I N T R A T H O R A C I C T U M O U R S

A REVIEW OF THE LITERATURE AND A STUDY OF THIRTY FIVE CASES OF PRIMARY INTRATHORACIC CANCER.

by

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INTRODUCTION.

In recent years the subject of intrathoracic tumours has received increasing attention. The apparent increase in the incidence of cancer of the lung, out of proportion to that of malignant disease of other organs, has been recognised by observers from all parts of the world. Intrathoracic lesions manifested by symptoms such as cough, expectoration, haemoptysis, have been so readily diagnosed as phthisis without much consideration of the possibility of the presence of new growth, that it was thought that it would be of interest to study more closely the cases which have been recorded and the literature surrounding neoplasms arising within the thorax.

Personal contact with a few instances in which the symptoms, at first suggestive of pulmonary tuberculosis but proved by subsequent careful investigation to result from benign intrathoracic growths, has to a large degree stimulated this study. It seemed, from these examples, that many patients suffering from similar lesions may have been condemned to lives of invalidism in Sanatoria until a fatal termination was reached, in whom more complete investigation with a more accurate conception of the details and modes of securing a diagnosis might have lead to successful treatment.

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In the standard text book "Practice and Principles of Medicine" (Osler and Macrae) published in 1923 this subject is given scant attention, and only a few pages are allotted to its discussion. Within the last few decades the bibliography has grown to such an extent that it is now possible to review all aspects of a number of cases of intrathoracic tumour sufficiently large to allow deductions to be made with regard to their main features. It is thus intended to review the more important contributions to the literature in order to ascertain the present state of our knowledge, and, by this means, to indicate in some measure the lines on which further progress is likely to be made in dealing with intrathoracic neoplasms.

The field under review will include benign and malignant new growths arising primarily within the chest. Those originating from the thoracic wall, from the oesophagus, the pericardium, and the heart will not be considered except with regard to differential diagnosis and other associated features. Enlargements of the thymus gland of non-neoplastic nature will be discussed in view of the confusion which may arise in the diagnosis and treatment of thymic new growths. With regard to the rarer forms of tumour, most of the examples recorded in the literature will be mentioned though it is not intended to form a complete collection of/

of each series. The scope of the review will include the incidence, aetiology, pathology, symptomatology, diagnosis and treatment of the various types of benign and malignant neoplasm arising within the chest.

A report of thirty-five cases of intrathoracic tumours which were submitted to autopsy within the last five years at the Royal Infirmary, Edinburgh, is added. A discussion will be made of the clinical and pathological details and a summary will be given of the more striking features which these cases portray.

HISTORICAL FEATURES.

Morgagni seems to have been the first to have given a definite account of pulmonary tumours. He described the findings at the autopsy on a man, sixty-six years of age, whose lungs and mediastinum were matted by a growth. Other similar cases were reported in 1766 as "pleural pneumonia". Boyle, in 1810, recognised the entity of pulmonary cancer in his report of three cases of "phthisie cancereuse". Nine years later, Laennec described the condition of "encephaloid of the lung" in his immortal work, "l'Auscultation Médiate". About this period several English observers also recognised the same condition. Amongst them were Langstaff, Bright, Harrison, Hughes, Taylor, Machlachlan, Bell (1820-1840), whilst Herzog, Oettinger, and others drew attention to the subject in Germany.

In 1843 Walshe mentioned "cancer of the lung" in his book "Physical Diagnosis of Lungs". Stokes, who wrote "Diseases of the Chest" in 1837, mentioned the fact that frequent and severe attacks of bronchitis resisting usual treatment should cause suspicion of a malignant tumour. He gave a clinical description of the diagnosis of pulmonary cancer. Virchow added to the study of the pathology in his writings produced in 1853. Some twenty years later Waldeyer advocated the/

the epithelial origin of cancer of the lung. The pathological considerations were further propounded by Langhans, Chiari, Epstein and Stilling who believed that the growths arose from the mucous glands of the bronchi. In 1891 Ehrich described the origin from the epithelium lining the bronchi.

The first large collection of cases were reported by Adler in 1911 when he published his classical account of 374 cases of intrathoracic tumour. Since that time the writings have been numerous and the bibliography has increased on every side so that a comparatively large series can be studied. The literature gives evidence of progressive improvement in those means of diagnosis which were denied the earlier workers. Of recent years many contributions have included descriptions of the surgical removal of intrathoracic tumours, and during the present century radiotherapy has attained a prominent position as a means of treatment.

To Sauerbruch and others on the Continent, to Lilienthal, Heuer, Graham, and Jackson amongst those in the United States, and to Morriston Davies and Tudor Edwards of the British workers we owe many of the advances of modern times which have made the thorax an accessible field, diagnosis more definite, and the cure of intrathoracic neoplasms more frequent.

BENIGN TUMOURS OF THE LUNG.

There are remarkably few recorded cases of benign intra-pulmonary tumours. In his text book, Lilienthal mentions lipoma, chondroma, fibroma, osteoma, fibro-papilloma, adenoma of mucous glands, and dermoids. He states that they are all rare but are found occasionally post-mortem or during operation, that dermoid cysts may be found within the lung and are the type most frequently dealt with by operation. Reisner has collected reports of twenty-six benign bronchial neoplasms, eleven of which were removed by means of the bronchoscope and the remaining fifteen were found at autopsy. Various other cases have been recorded and will be mentioned, though it is not intended that a complete collection be formed. At least four cases (Ashbury, Rösner, Ewart Martin, Myerson) may be added to the series quoted.

Lipomata are found most commonly as sub-pleural tumours giving rise to few or to no symptoms and often discovered incidentally during post-mortem examination. They may be round or flattened fatty nodules, sessile and occasionally pedunculated, occurring singly or as multiple small tumours. Adipose tissue is also found in association with the mixed tumours. Lipomata may rarely cause obstruction of a bronchus. Rokitansky has/

has recorded one case where the left lower bronchus was obstructed, while in the case of Feller the right middle bronchus was occluded by a lipoma-like tumour.

Fibromata are among the more commonly occurring benign tumours, six being present in Myerson's series of intrabronchial growths. Usually in the form of multiple small nodules situated beneath the pleura or in the region of the larger bronchi, they may produce few or no symptoms. Of those growing into the lumen Yankauer records one case, and removed the tumour in the case described by Ashbury. Wessler and Jaches, Pfeiffer, Jackson, Zinn, Burrell and Traill (by Negus) have each reported cases in which the fibroma has been removed with the aid of the bronchoscope, while others have been noted at autopsy (Krack). All of these have been small and pedunculated. Eppinger has described a large tumour, 20 x 12 x 20 cms., which caused death. The origin was said to be the pleura. A similar case has been observed by Schultz.

Chondromata occur with greater frequency in the trachea than in the lungs (Ewing). They are found as ecchondroses in the upper respiratory tract, in the larynx and growing from the tracheal rings. Ecchondromata may be multiple, situated at the root, in the parenchyma, or on the pleura, or they may occur singly. Calcification or ossification may occur in them.

Siegert/

Siegert and Blecher have reported cases where the growth has projected into a bronchus, the former into the right main bronchus and the latter into the left bronchus. Patterson quotes von Eicken who, in 1907, removed an ecchondroma of the left main bronchus of a man aged 41 years, and Speiss who dealt with a similar case in 1917. Multilobular growths composed of hyaline cartilage may rarely be situated deeply within the lung. Davidson quotes Enzières and Pagès who described a hard nodule, the size of a walnut, found post-mortem in the middle lobe of the right lung of a woman, aged eighty years, who had died of pneumonia. The tumour was composed of hyaline cartilage, connective tissue fibres and some adipose tissue. The same authors mention a similar tumour of larger size, 15 x 11 cms., reported by Gayet (Thèse Riboul, Lyons).

Osteochondromata and osteomata are rare tumours found chiefly in the aged as multiple growths situated round the bronchi. Heuer mentions that osteomata have been seen in the forms of spicules or plaques and quotes the description by Kummell of an osteoma, spherical in shape and of the size of a fist. Virchow noted a similar tumour in the left upper lobe. The osteomata are more probably of the nature of heterotopic ossifications than true neoplasms. Graham emphasises the fact stated by Le Count that remarkable growth of bone may occur in the lungs secondarily to sarcoma of/

of the long bones. It is not usual however to find calcium in the pulmonary metastases from bone tumours. The pathology of these ossifications is as yet controversial.

Angioma of the lung is exceedingly rare. One example has been noted by Hedinger, and Tuffier exposed such a tumour under the impression that it was an abscess. He treated the growth by applications of ferric chloride. Ewart Martin has recorded the finding of an angioma during bronchoscopy. The tumour extended from the anterior wall of the trachea over the carina for a quarter of an inch down the right bronchus. There had been recurrent attacks of haemoptysis for thirty-two years, and the patient had had treatment in Switzerland under the assumption that she was suffering from pulmonary tuberculosis.

Tumours composed of a mixture of tissues have been observed both within the bronchi and in the parenchyma of the lung. Forkel has described a fibromyoma the size of a lemon situated in the left apex and discovered incidentally at autopsy. Myerson has added to Reisner's collection a bilobed tumour, removed by the aid of the bronchoscope, which on examination proved to be a fibrolipoma. This growth had caused almost complete atelectasis of the left lung by occlusion of both bronchi. Reisner includes a lipo-chondroadenoma amongst the benign intrabronchial tumours. It is possible that some of the less

definite/

definite and less carefully examined "mixed tumours" may be of a teratoid nature.

Benign epithelial growths are of importance in view of their relation to carcinoma. From the analogy to epithelial growths elsewhere, the chances of the development of a malignant lesion in a pre-existing benign epithelioma may well be evident. The fact that such innocent tumours do exist and can be diagnosed during this stage should encourage the institution of steps for their removal before the onset of malignancy. Myerson's collected cases include four adenomata which had been discovered at autopsy, one tumour which was thought to be benign but which showed evident carcinoma on histological examination, and six polypi or polypoid tumours. He includes the case of Radestock, who reported the blockage of the left main bronchus by a tumour resembling thyroid tissue and stated to be an aberrant thyroid lobule. To this series may be added a case described by Rösner who reported the findings at autopsy on a woman, aged 52, who had died as a result of bronchiectasis due to obstruction of the right bronchus by a polypoidal benign adenoma. Davidson quotes Linser who discovered an adenoma occurring within the lung. This, however, may have been a portion of a teratoid tumour.

In the polypoid intrabronchial tumours recorded by/

by Kreglinger, Kirch, Heck, and Malkowitz, malignant changes were detected. Especially in the case of the first-named it was presumed by a history of eight years duration that the original nature had been benign.

Intrathoracic teratomata are found much more frequently in the mediastina than in the lung, but cases have been recorded where their intrapulmonary origin has seemed to be definite. Lilienthal states that within the lung they may become large and compress the pulmonary tissue. They may contain also malignant elements. Like teratomata elsewhere they may be cystic or solid. Borelius and Sjovall describe the removal of a tumour of this nature and others have been reported, but there are few cases where the origin has been definitely intrapulmonary. In view of this dubiety and the known frequency of teratomata in the mediastinum these growths will be discussed under mediastinal tumours.

C Y S T S.

The literature contains few references to true cysts of the lung. Dermoid cysts and teratomatous cysts may rarely be found but, as has been stated above, their intrapulmonary origin is uncertain. Simple serous cysts have been noted. Lilienthal describes a cyst within the lung having a lining of hyaline connective tissue and containing brownish-coloured fluid. This would not appear to be a true dermoid cyst. Neuhof has recorded the case of an intrapulmonary cyst, lined by ciliated epithelium and containing infected material, in close association with the wall of a bronchus. Their origin has been cited as bronchogenic, a retention cyst having been formed by the embryonic pinching off of a bronchus or bronchiole. Grawitz claims an interstitial origin from faulty anlages of the lymph vascular system.

A number of examples of congenital cystic disease of the lung have been described. Miller has reported two cases. The first occurred in a child, five weeks old, which developed a spontaneous pneumothorax associated with cyanosis and dyspnoea, and relieved by thoracentesis. After a second attack, the third terminated fatally at the age of five months. There was no autopsy. His second case presented a similar history/

history, and the lung examined after death was found to contain numerous peripheral cysts lined with flattened epithelium communicating with each other, but with an alveolus at one place only. A similar case is reported by H. Meyer. Stoerk observed that the cystic condition may be present as a mass attached to one lobe, to which he gave the name "Fetal cystic bronchial adenoma". Wechsberg has described a similar mass attached to the oesophagus. Koontz has collected a series of 108 cases of congenital cysts including those derived from the trachea and oesophagus. Of these, thirty-one occurred in infants under one year of age, and in 25% both lungs were affected. In the remaining cases the left lung was the more common site. Two types are described. In the first group there is a dilatation of the bronchi, the cyst having a wall of concentric muscle fibres and cartilage, and a lining of stratified ciliated epithelium. The second type resembles in structure emphysematous bullae. Esch describes a congenital adenoma of the lower right lobe of a child which had lived for one and a half hours. The lobe contained gland-like cavities of varying size lined with a single layer of cubical and cylindrical epithelium. The walls of the cavities contained muscle and collagenous tissue. There was no cartilage but the appearance would seem to conform to the first group of Koontz. Kerley has published an example of bi-

lateral/

bilateral fibrocystic disease of the lungs which caused cough and increasing dyspnoea for a year before death of a woman aged thirty-two years. The X-ray appearance was of a meshwork suggestive of lymphangitis carcinomatosa. The lungs showed generalised cysts varying in size from that of a pea to about 1¼ inches in diameter. They appeared to contain gas under pressure, were separate from the lung tissue, and showed no exudate or desquamation of the lining cells. They conformed to some extent to the types included in the second group described by Koontz.

Couvelaire has suggested the same factors of origin as are associated with congenital cystic disease in the kidney and other organs. Virchow regarded the cystic spaces as dilated lymph vessels.

HISTOLOGY.

The detailed histology of these tumours does not require special mention. The simple growths, fibroma, lipoma, chondroma need no description. The nature and possible modes of production of the osteoma group have been indicated. Endotheliomata will be described more fully under pleural tumours.

Of the epithelial growths, the adenomata may be exemplified by Reisner's case where a polypoid tumour occluded/

occluded a bronchus. The section showed columnar epithelium in alveolar formation indicating the origin from the mucous glands or from duct epithelium. The surface epithelium was intact except for areas of post-mortem desquamation and presented no ulceration. There was no transgression of the basement membrane or of the surrounding tissues. The polypi differed in no respect from their usual nature, consisting of a connective tissue core covered by normal epithelium. The polypoid tumours of Kreglinger, Kirch, Heck, and Malkowitz showed proliferation of epithelium and mitosis suggestive of malignant change in previously benign polypi.

The pathological changes in the lung depend on the mechanical effect of the tumours, on the surrounding reaction, and on the degree of superadded infection. Where bronchial occlusion was present the distal lung tissue was collapsed in some cases, while in others the common features of bronchiectasis were striking. In Reisner's case there was, in addition to bronchiectasis, a chronic empyema and a broncho-pleural fistula. Further, haemorrhage had occurred from the rupture of an aneurysm of a branch of the pulmonary artery. This case is especially instructive as it illustrates the sequence of pathological changes which may be associated with, and result from, a small benign tumour.

SYMPTOMATOLOGY.

The presence of symptoms depends largely on the site of the tumour. The small tumours at the periphery or in the central portions of the lungs usually give no indication of their presence. Larger tumours, such as the fibroma described by Eppinger, may become evident in virtue of their size and the corresponding compression of the lung. Mechanical obstruction of the bronchi, by occlusion from within, or by pressure from without, have led to atelectasis and to bronchiectasis. In Ashbury's case, where occlusion was due to a pedunculated cellular fibroma, there were recurrent attacks of atelectasis with dyspnoea and cyanosis. So vague were the findings on clinical examination that Myerson's patient was regarded as neurotic until massive collapse of the left lung was indicated by a radiogram and the tumour was revealed by bronchoscopy. In a few cases of bronchiectasis the sputum was blood-stained but this was not attributed to the tumour so much as to the pathological complication. In Ewart Martin's example of angioma there had been recurrent attacks of haemoptysis from the age of eighteen until bronchoscopic examination at the age of fifty. Burrell and Trail noted continuous coughing of blood for eighteen weeks in a case of intra-bronchial fibroma.

TUMOURS OF THE PLEURA.

Benign tumours of the pleura are extremely rare. Lipomata, fibromata, and chondromata do occur, while mention may be made of a group of "mixed" and more malignant types such as chondromyxoma, chondrosarcoma, and fibrosarcoma. Little is stated in the literature about true sarcoma of the pleura which will be discussed under endothelial tumours.

Lipomata, fibromata, and chondromata occur usually under the visceral pleura. It is doubtful whether they arise from the tissues composing the pleura or from those of the lung. It will suffice to say here that they may be single or multiple, usually remain small, and give rise to few or to no symptoms. The large fibroma recorded by Eppinger and already mentioned may have originated from the pleura. Kornitzer has described a tumour of the nature of a leiomyoma growing from the pleura of a patient who presented an endothelioma of the pleura of the other lung. Roberts has on record an encapsulated endothelioma of the right lower lobe which was removed at operation. There is, however, no definite statement that the nature of this tumour was benign, though this may be inferred from its encapsulation.

The "mixed" growths are usually malignant and tend to recur after removal. In most cases they originate/

originate in the chest wall especially from the ribs and costal cartilages, the vertebrae and the inter-vertebral discs, and do not concern the present discussion.

By far the commonest of the pleural tumours, that designated endothelioma has received considerable attention from pathologists. In 1905 Bloch reported 63 pleural neoplasms of which 47 were said to be of the nature of endothelioma, the remaining 16 being classified as sarcomata. In the light which more recent work has shed on cytology these latter tumours might be considered to be endotheliomata. In 1914 Clarkson reported 41, and Rosenbaum 62 cases of pleural endothelioma. From his personal experience of thirty intrathoracic tumours, Heuer found six to be of this nature, while Maxwell recorded five growths of the pleura out of 226 neoplasms within the chest. Of these, two were diagnosed as endothelioma and one as mixed-cell sarcoma. Keilty found nine cases of primary endothelioma of the pleura during the performance of 5,000 autopsies. Other figures of incidence include three cases in 3,000 post-mortem examinations conducted at the University of Minnesota during twelve years. Levinny recorded the occurrence of a spindle-cell sarcoma of the pleura in a woman aged 43 years. He was able to find in the literature only five similar cases. Subsequently Macmahon and Mallory described a pleural/

pleural fibrosarcoma in a man aged 71. From these references it will be seen that malignant tumours of the pleura are extremely rare.

The origin of the endothelioma has been ascribed to two sources. Wagner, Volkmann, Adler, and others have emphasised the affection of the subpleural lymphatics in the early stages, and relate the origin of the growth to the cells lining these vessels. Benda and Gurrman are mentioned by Ewing as being able to trace the source of the tumours to the cells lining the pleura. From the nature of the growths and from their mode of spread, it would seem possible that they may arise from both sources, those taking origin from the lymphatics becoming invasive along the subpleural and interlobar plexuses, while the tumours arising from the serous lining cells may form the more nodular superficial types. No close distinction can be formulated however. It has been claimed that the process may be the sequela of an inflammatory lesion whereby malignant growth becomes superimposed on a chronic pleurisy. This factor has been applied with more or less substantiation to malignant disease in most organs. Ribbert designates the endothelial tumours as carcinoma in the belief that the cells lining the coelomic cavities are of epithelial nature. Others hold that there is little support for this view on morphological grounds.

Two/

Two gross types have been described. Growth may be diffuse, usually invading the lung along the septa, producing irregular nodules and masses within the lung and secondary deposits in the mediastinal glands, liver and distant organs. The circumscribed type is less common extending locally and often eroding the diaphragm and ribs with less tendency to metastasis. Invasion of the lungs may be absent (Wagner) and the costal pleura alone may be affected (Scaglioni). In some cases however, the visceral and parietal layers of pleura become fused to form a diffuse mass which compresses the lung from without. Infiltration may involve the sympathetic or phrenic nerves, but the great vessels, pericardium, and oesophagus are not commonly affected. A sero-fibrinous or sanguineous effusion is usually present, diffusely as a prominent clinical feature or as localised collections of fluid.

The cells are of moderate size, flattened or polyhedral with relatively clear cytoplasm, pale vesicular nucleus and nucleolus. They are supported by a fine connective tissue stroma and may lie in rows or in alveoli, clinging to the walls of spaces in a characteristic manner. Plexiform arrangements have been seen. Adenomatous appearances are not infrequent and are often so pronounced as to render pathological diagnosis doubtful. Mucus containing

cysts/

cysts may occur but there is not the same production of gelatinous material as may be seen in the peritoneal endotheliomata.

In the five cases fully recorded by Maxwell, three affected the right side and two were situated on the left side. In three cases the lung was not involved although the diaphragm was infiltrated. Metastases were found in the mediastinal glands and in the liver in two examples, and in the suprarenal gland and pericardium in one instance. Heuer's personal cases included three of the diffuse and four of the circumscribed type. In three cases operation for their removal was undertaken. The first tumour, almost filling the upper half of the right chest, was red, succulent, pulsating, closely incorporated with the upper lobe under the pleura and fixed to the mediastinum. The second showed erosion of the seventh and eighth ribs by a tumour the size of a lemon lying in the costo-phrenic sulcus. Heuer's third case, which had remained well and apparently cured two years after operation, consisted of a pulsating mass the size of a hen's egg, presenting as a swelling below the left scapula.
In the former two cases there was subsequent recurrence of the growth. All three tumours were diagnosed as endotheliomata on histological examination, and have been described as fair examples of their types.

Of Maxwell's cases one was found to be a "mixed-call sarcoma" but this appearance has been seen in other endotheliomata which have shown sarcomatous qualities - a fact borne out by several authorities (Miller and Wynn, Waldeyer, Zeigler). Edwards records the successful removal by lobectomy of an endothelioma of the right lower lobe. There were no pleural adhesions, and no involvement of the mediastinal glands had occurred.

From the account given above it may be inferred that endothelioma of the pleura is a rarity. In conclusion reference must be made to a recent contribution. A masterly paper by Robertson has presented the subject in a new and somewhat heterodoxical manner. After discussing the reported cases, the difficulties which have been encountered, and the various lines of thought which pathologists have adopted, this author has drawn the inference that only "the sarcomas can be classified as primary malignant tumours of the pleural tissues, and that all other growths are secondary, representing extensions, implantations, or metastases from an unrecognised or latent primary source, usually in the lungs". He describes four personal cases which conform to the description of pleural endothelioma given above. He also reports the occurrence of what appeared to be an adenocarcinoma of the pericardium in illustration/

illustration of the power of differentiation of endothelial cells. Careful examination however, proved this growth to be a metastasis from a small adenocarcinoma of a bronchus. It is to this striking primary error that attention is drawn. One of the most prominent reasons for the inference of this writer lies in the theory that many diagnoses are made on a quantitative basis, the origin of a tumour being decided according to the site and type of maximum growth. This theory, however, has obvious and definite limits. It is a matter of common knowledge that a small insignificant primary tumour may, and frequently does, give rise to metastases which, by virtue of size and resulting symptoms, completely outweigh the consideration of the initial growth. While he acknowledges that this source of fallacy is widely recognised, Robertson is still "firmly convinced that, at least so far as the pleura is concerned, no diagnosis of primary carcinoma, mesothelioma or endothelioma either from lymphatic endothelium or serosal surface cells, can ever be justified on any logical ground".

In support of the latter statement it is generally allowed that metastasis in a serous membrane tends to produce a widely spreading growth as is illustrated by the implantation tumours of the peritoneal cavity. One may also consider the analogy of tuberculous disease of the mediastinal glands. Extension of the disease/

disease may occur slowly but definitely along the peri-bronchial lymphatics, perhaps reaching the pleura without involvement of the lung parenchyma, to become evident clinically as an insidious effusion and pathologically as a tuberculous pleurisy. It is difficult to entertain this analogy in those instances of peripheral endothelioma where careful search has excluded the presence of any other growth and no sign of lymphatic infiltration from the central or hilar regions has been evident. Even with a retrograde lymph spread it is not easy to reconcile the appearances afforded by an endothelioma of the pleura extending along the lymphatics towards the root of the lung with a theory which holds that the peripheral growth must be secondary to a carcinoma of a main bronchus or to some other central tumour. Nor is this picture compatible with metastasis carried by the blood, as spread by the blood stream would involve other organs rather than the pleura alone. Robertson's assertions have not as yet found general support and it would appear to be unwise at this stage to dismiss to other categories those tumours which have hitherto been classified as pleural endotheliomata.

SYMPTOMATOLOGY./

SYMPTOMATOLOGY.

Little need be said about the special clinical features of pleural growths which correspond closely to those of secondary pleural involvement. The latter will be discussed in detail under the general study of symptoms of intrathoracic tumours.

The onset of symptoms is usually late in the course of the disease. The insidious growth may have become so large as to compress the lung to a considerable extent before any definite symptom is noticed. There may be neuralgic pains in the side of the chest or merely a feeling of fulness and increased weight. Dyspnoea usually becomes marked and, with steady weakness and loss of weight, may be the only complaint. There may be localised bulging followed by retraction of the interspaces. Marked dulness on percussion with diminution of sound conduction is due both to the presence of the tumour and to the fluid which so constantly accompanies it. Examination of the pleural fluid will be discussed at a later stage. Emaciation is often marked and death usually follows an attack of pneumonia.

T R A C H E A.

BENIGN TUMOURS.

Benign tumours of the lower part of the trachea are exceedingly uncommon. Small chondromata have been seen arising from the tracheal rings and forming elevations of the surface within the lumen. Ribbert and others have recorded osteomata arising in the same manner. Polypi may occur but there is little note of other types of growth in the records.

MALIGNANT TUMOURS.

Carcinoma of the intrathoracic portion of the trachea is also extremely rare. Figi found five cases in the records of the Mayo Clinique from 1918 until 1930. Of these, three affected women and two occurred in men. From a study of the literature it has been possible to find other reports by Vinsen, Moersch and Kirklin, Grove and Kramer, Maxwell, Torres and de Azevedo, and Stenstom. The tumours were found in patients of middle age. Of the five cases described by Figi, three were squamous cell carcinoma, one was an adenocarcinoma and the fifth growth is recorded as unclassified carcinoma. Stenstom's case was a basal cell carcinoma, and the two examples reported by Torres and de Azevedo were both of squamous cell carcinoma/

carcinoma. The pathology shows no marked variation from that to be described in connection with the bronchi. In Stenstom's patient involvement of the right recurrent laryngeal nerve had occurred and the condition had been diagnosed as aortitis. Neither tumour of Torres and de Azevedo had invaded the lungs though one had extended to the mediastinal glands.

Somerville Hastings mentions that Killian was the first surgeon to remove a sarcoma from the trachea by means of the galvano-cautery. Apart from the types noted above there is little mention of others in the literature.

In most instances the symptoms were primarily sensations of tickling in the throat and cough. Later slow suffocation usually terminated by pneumonia.

MALIGNANT TUMOURS OF THE LUNG.

INTRODUCTION.

As a site for cancer, the lung has received increasing attention during the last few years. While the frequency of malignant disease generally seems to have become greater, the incidence of pulmonary carcinoma has shown an apparent increase far beyond ordinary proportions.

Statistical evidence abounds from most of the larger cities of the world and has been submitted to thorough analysis by numerous observers. While mere figures cannot represent an exact picture of all of the various features of the disease they are nevertheless helpful in the comparison of the findings of many authorities. For this reason, a series of tables, some adapted and modified from the literature and others compiled from the available records, have been drawn up in order to facilitate the study without the intention of narrowing the review but of keeping the basis as wide as possible.

INCIDENCE.

It has been evident that benign tumours of the lung and tumours of the pleura are of comparatively rare occurrence. The inclusion of these growths will have/

have little effect on any figures concerning a large number of pulmonary neoplasms. It has been thought necessary to mention this fact because some of the figures quoted in the tables under primary carcinoma of the lung may include a few cases of extra-pulmonary growth or of benign tumour. As has been explained, however, the statistics of "primary carcinoma of the lung", "intrathoracic neoplasms", "pulmonary cancer", etc., are identical within fairly wide limits. So far as it will be possible the term of choice will be "carcinoma of the lung". The existence of sarcoma is sufficiently doubtful and, in any case, of such extreme rarity that the terms employed may be understood to include all primary malignant growths of the lungs and bronchi. Most of the available figures are represented in the tables while those of special note will be discussed in the text.

Figures relating to the incidence of carcinoma of the lung have emanated from centres of wide geographical distribution. It is a fact of obvious significance that in almost every instance the incidence of this disease has shown a marked increase. How far these figures represent a true increase can only be decided after consideration of changes in nomenclature, more accurate diagnoses, and other factors.

In Germany the statistical studies of Kikuth and Hanf/

Hanf have shown an example of the marked increase of cancer of the lung during the last three or four decades. Kikuth examined the figures at the Eppendorfer Hospital in Hamburg, representing a period of thirty-five years prior to 1923, and found a total of 246 cases of primary pulmonary carcinoma at autopsies on 59,982 patients. His observations indicated the remarkable rise of incidence most evident during the last third of the period, during which 146, that is more than half the total, cases were observed. Kikuth found that in 1923 the lung ranked second on the list of frequency of special sites affected by malignant growth and that pulmonary cancer was one third as common as carcinoma of the stomach, making 9.5% of the total cases of cancer. This high percentage is significant of the incidence. Other figures produced by Continental workers include those of Wahl of Berlin, who, from more than 25,000 autopsies, found 13.01% of total cancer to be intrathoracic during the five years 1922-1926. This figure is one of the highest in the records. Biberfeld, from the same city reports the incidence from 1917-1921 inclusive as 6.2% of total cancer. The discrepancy between these figures obtained from the same locality lies in the different factors which will be discussed later. Lubarsch, in an analysis of cases throughout Germany in 1920 and 1921, found/

found carcinoma of the lung to represent 5.4% of all cancer. Hanf, whose statistical studies are among the most complete of the investigations of the recent Continental workers, found an increase in the same proportions as those of Kikuth, and commented on the yearly fluctuation in the number of autopsies as a factor worthy of consideration. Her view, however, is that both actual and relative increases have occurred in the incidence of lung cancer. Ferenczy and Matolcsy have provided the records of the largest number of autopsies which have been studied, and their results are worthy of note. Out of 62,602 autopsies from 1896 to 1926 a steady increase is noted in the percentage of cases of cancer which were intrathoracic, the figures being 5.4% for the first five year period and 10.3% in 1924. Similar figures may be quoted from numerous other Continental authorities.

In the United States the statistics are comparable but there is not so marked an increase as there appears to have been in Germany. Rosahn of Boston noted 6.98% of all cancer to be situated in the lung. This figure was obtained during the years 1920-1928. For the previous ten years, 1910-1919, the figure was 4.39%. At the Cook County Hospital, Grove and Kramer found that .57% of 3,659 autopsies, performed during the years 1917-1924, revealed cancer of the lung. From the/

the Department of Pathology of the University of Minnesota, Barron records no cases in 1, 333 necropsies from 1899 to 1911, while in 1919-1921 .9% of 1,003 autopsies revealed primary pulmonary cancer. Klotz, of Toronto, shows similar figures, 1% of cases examined after death being carcinoma of the lung.
In Buenos Aires, Strada reports the incidence at autopsy to be .22% and cancer of the lung to be 18.75% of total cancer. These figures are low and high respectively but their value is less owing to the small number, 558, of autopsies which they concern.
Hoffmann has studied the official figures in the United States registration area. He found a steady increase in the number of deaths resulting from lung cancer. The numbers given per 100,000 of the population were 0.6 in 1914, 1.6 in 1924 and 1.7, 1.8, and 1.9 in the three succeeding years.

With regard to British figures, perhaps the most useful contribution is that by Georgiana Bonser of Leeds. After careful collection and tabulation of records from all parts of the world, this observer finds the results of the Leeds autopsies to differ from the average findings in respect of the incidence of pulmonary cancer in earlier years. While the recent frequency corresponded to that elsewhere, Bonser found that 1.05% of autopsies of the years 1893-1897 were cases of carcinoma of the lung, and 6.3% of all examples/

examples of cancer were intrathoracic. These figures are greater than the general records obtain, and it would appear that there has been no evident increase of the frequency of lung cancer in this locality. Bonser gave a summary of most of the available figures and Table I is a modification of tables adopted from her paper. The records of St Bartholomew's Hospital analysed by Maxwell and Nicholson show results similar to those of Leeds with regard to the early periods during which the incidence is somewhat high. The frequency has greatly increased, and the authors state that in the period 1924-1928 one seventh of the cancer cases found in the post-mortem room at their hospital were carcinoma of the lung. Levy Simpson has recently published the results of his study of the London Hospital records of the years 1907-1925. From both post-mortem and clinical diagnosis the increase in incidence of lung cancer was proportionately greater than that of cancer throughout the body. His figures given in Table II show the rise based on post-mortem examination. The combined clinical and post-mortem data are worthy of consideration. Taking the first and last four year periods for comparison, the years 1907-1910, with 2,702 cases diagnosed clinically as cancer, showed 1.52% to be malignant disease of the lung, while in the period 1922-1925 of 3,071 cases of cancer/

cancer 3.65% were pulmonary tumours. These figures are relevant to the discussion which will arise with regard to the effects of recent improvements in diagnosis. The increase of lung cancer would seem to be real and independent directly of such improvements in clinical and pathological diagnosis. Simpson's figures do not show the marked increase which is evident from the German statistics, but they do nevertheless indicate the greater frequency in recent years from both post-mortem and clinical observations. In Aberdeen, Shennan found that during the years 1914-1927 the incidence of primary cancer of the lung at autopsy was 1.7% Duguid of Manchester examined the records of 10,780 post-mortem examinations. In the four years 1886-1890 the percentage of cases at autopsy which were cancer of the lung was .24. For the period 1921-1925 the corresponding figure was 2.57 - a remarkable increase. Davidson has published the statistics of the Brompton Hospital. The percentage of cases at autopsy (561 from 1918-1928) which were malignant disease of the lung has steadily increased from 16% to 29.6%, the fluctuation of the annual figures being slight. This hospital is concerned almost entirely with diseases of the chest.

Shaw Dunn and Powell White have reported the results of the investigation by the International Cancer/

TABLE I. (continued).

Author.	Locality	Total Autopsies	5 Year Periods commencing	% of autopsies where were intra-thoracic cancer.	% of total cancer which were intrathoracic.	
Breckwoldt	Hamburg	12,432	1914-1917 1922-1925	.46 .52	5.11 3.45	)
Marchesani	Innsbruck	13,367	1887-1896 1916-1922	.26 .3		) No marked increase.
Berencsy and Wolff	Budapest	19,908	1894-1898 1919-1922	.11 .25		)
Bonser	Leeds	15,520	1893-1897 1923-1927	1&05 1.17	6.3 7.97	)
Average of percentages			Prior to 1910 After 1920	.27 1.0	3.9 8.4	

TABLE I. FIGURES OF INCIDENCE OF INTRATHORACIC CANCER. PRIMARY CARCINOMA&
(Modification of tables of Bonser G. (Leeds) Journal of Hygiene 1928).

Author	Locality	Total Autopsies	5 Year Periods commencing	% of autopsies which were intra-thoracic cancer	% of total cancer which were intrathoracic.
de Vries	Holland	8,000	1910	.1	
			1925	.95	
Brandt	Riga	13,179	1901		1-2%
			1921		10-11%
Wahl	Berlin	25,134	1895	.44	4.3
			1922	1.69	13.01
Biberfeld	Berlin	36,428	1897	.36	4.8
			1917	.72	6.2
Hanf	Berlin	30,380	1903	.2	2.58
			1921	1.28	7.2
Eichengrun & Esser	Cologne	13,318	1902	.36	6.26
			1919	.81	9.14
Seyfarth	Leipzig		1900		5.01
			1919		8.75
Rau	Dresden	10,413	1909	.92	7.5
			1914	1.27	11.2
Kikuth	Hamburg	59,982	1889	.02	1.95
			1919	.86	11.2
Berblinger & Bilz	Jena	8,056	1910	.34	2.2
			1920	.99	8.3
Materna	Troppau	5,191	1912	.11	2.08
			1921	.57	8
Holzer	Prague	29,762	1895	.19	2.62
			1920	.70	9.23
Ferenczy and Matolcsy	Vienna	62,802	1896	.15	5.4
			1920	.71	10.3 (in 1924)
Staehelin	Basel	16,759	1900-1911	.2	2.1
			1915-1923	.63	5
Klotz	Toronto		1910-1920	.5	
			1921-1927	1.0	
Barron	Minnesoto	4,362	1899-1911	0.0	
			1919-1921	.9	
Duguid	Manchester	10,780	1886-1890	.24	
			1921-1925	2.57	

Cancer Conference of 1928. The records of six centres were studied (Birmingham, Edinburgh, Glasgow, Leeds, Manchester and University College Hospital, London). It was shown that the .94 incidence at autopsy in the period 1903-1907 rose to 1.69% in the years 1923-1927. It will be seen from Table I that the greatest increase evident from British, and indeed from all figures included, has occurred at Manchester.

A consideration of the factors which influence these records must be undertaken in order to arrive at some conclusion. The value of statistics has been well discussed by H. Gideon Wells who has pointed out the various fallacies which may arise in their interpretation. He has laid special stress on the selective factors of locality and type of hospital, and it has been shown that the hospital statistics may differ widely from those of the registration authorities. Lubarsch is quoted as saying that, in his opinion, half the cases of cancer in Germany are not being reported in view of the necropsy records showing 9.2% of cases to be cancer against 5.68% as recorded by vital statistics.

It is obvious that figures based on post-mortem evidence are the most reliable. The gross pathology has not changed, and the characters which concern diagnosis/

diagnosis have remained much the same throughout the last fifty years. As most of the available figures are calculated from results obtained at autopsy it may be advantageous to deal with these at somewhat greater length. Change of nomenclature has undoubtedly played a part; many cases previously regarded as sarcomata are now classified as carcinoma of the lung. In terms of intrathoracic cancer however, most of the statistics quoted in Tables I and II include all these tumours. The limitations of individual error in pathological diagnosis must be much the same throughout the centres.

Selective factors of locality and type of hospital may be evident in some instances. It may be supposed that fluctuations in age of a population supplying patients to a specific institution would show a corresponding effect on the statistics, a lowering of the ages producing fewer cases of malignant disease. It must be extremely uncommon for such fluctuation of age to be sufficiently great to influence the incidence of cancer to the extent which has occurred in most localities. In the teaching hospitals there is considerable selection of cases for post-mortem examination and the presence of special departments for thoracic disease may influence the figures. For the latter/

TABLE II. INCIDENCE OF PRIMARY CARCINOMA OF LUNG.

(Various figures adopted from literature.)

Author.	Locality	Total Autopsies	Period.	% of autopsies which were Intrathoracic cancer.	% of total Cancer which were Intrathoracic.
Menetrier	Paris	-	1887-1917	-	10-12%
Shaw Dunn and Powell White	Birmingham	13,592	1903-1927	1.18	
	Glasgow	5,776	1903-1927	1.36	
	London	6,064	1903-1927	1.45	
	Edinburgh	10,687	1903-1927	1.14	
Playfair and Wakeley	London	3,183	1901-1923	.1	
Lavrinovitch	Petrograd	16,047	1905-1915	.38	
Grove and Kramer	Cook County Hosp. U.S.A.	3,659	1917-1924	.57	
Shennan	Aberdeen		1914-1927	1.7	
Strada	Buenos Aires	429	1914-1919	.12	8.47
		559	1920-1925	.22	18.75
Margarinos and Penna	Rio de Janeiro	1,531	-	.2	3.09
Casalo	Milan	2,658	1914-1925	.08	1.0
	Padua	11,968	1912-1927	.13	
Lubarsch	Berlin				5.0
Parish			1920-1924		1.7
			1925-1929		2.4
Rosahn	Boston U.S.A.	3,004	1910-1919	.44	4.39
			1920-1928	.89	6.98
Simpson	London	4967	1907-1910	.62	
		2356	1922-1925	1.69	
Maxwell and Nicholson	London	2484	1884-1888	.4	3.9
		1851	1924-1928	2.4	14.1

latter reason the Brompton Chest Hospital figures are much higher than the average. With few exceptions, of which this is one example, this special selectivity does not concern the results which are tabulated.

Hoffman has shown that in New Orleans the mortality rate due to lung cancer per 100,000 persons in the years 1919-1923 was 2.8 for the white population and .6 for the coloured races. This is an example of the discrepancies which may arise in figures from the same locality. As regards the official registration statistics the fallacies are widely known; the frequency with which death in cases of malignant disease is said to be due to other causes is an established feature. The references to statistics concerning diagnosis of pulmonary cancer during life, apart from those of Bonser, Levy and others, are so few that the attendant fallacies do not require more than brief discussion, most of the figures being based on information resulting from autopsy. The instances of pulmonary disease of this nature include the large number of middle-aged and old people in whom death has been recorded as due to phthisis, chronic bronchitis and cardiac failure, a considerable proportion of whom may possibly have had unrecognised malignant disease of the lung. It should be possible however, within a few years, to produce on a larger scale reliable hospital statistics of diagnosis of/

of carcinoma of the lung during life, the present thesis being that a large number of people die as a result of pulmonary cancer in whom the condition is either not suspected or is attributed to some diseases such as those given above. Bonser finds that in the years 1914 and 1927 the percentage of cases admitted to hospital and subsequently examined post-mortem was 5.7, with a similar figure in the intervening years, while the percentage of in-patients who were diagnosed as suffering from intrathoracic tumours (these may include the oesophagus) rose steadily from .127 to .253.

On the whole, the figures obtained from so many authorities, from localities varying widely in nature, concerning different races and types of industry, and applying chiefly to general hospitals, would seem to show a definite uniformity in their significance. Where it has been possible to compare these results with statistics of the incidence of cancer of the lung in the living the same signs of a real increase are apparent. Within reasonable limits it would seem safe to assume from figures of incidence based on autopsy reports recorded in Table I that cancer of the lung forms about 1% of all cases coming to autopsy and more than 8% of all malignant disease discovered post-mortem.

For purposes of comparison Table I is adapted from Tables/

TABLE III. LUNG - PRIMARY CARCINOMA.

(Modified from Table II & III in Journal Hygiene 28. 1928. (Bonser, Leeds))

INCIDENCE, ETC.

	1914	1927	1914-1927
Intrathoracic Neoplasms in the wards.	11	33	Steady increase
Admissions to wards.	8,667	13,048	Increase
% of cases which were intrathoracic neoplasms	.127	.253	Steady increase
% of cases admitted which were autopsied.	5.7	5.7	Constant
% of all deaths which were autopsied 1923-1927.	91.6		Increase
% of total autopsies which were cancer 1923-1927.	14.67		Fairly constant.
% of total autopsies which were intra-thoracic cancer 1923-1927.	1.17		No definite increase

Comment on Table III.

(1) Figures relating to autopsies are the most reliable and significant in view of more definite diagnosis.
(2) Incidence of cancer at autopsy appears to be constant.
(3) Incidence of intrathoracic cancer at autopsy would seem to show no increase in contrast to figures of other authorities.
(4) This latter fact is due to the high incidence in earlier periods whereas in later years the figure 1.17% is in close agreement with the average of the percentages 1.0% given in Table I.

Tables X and XI of Bonser's publication in the Journal of Hygiene. The yearly figures have been grouped into an early and a recent period each of five years, the single year noted indicating that and the subsequent four years. An attempt is made to show the increase of incidence of the number of cases of cancer of the lung found at autopsy, and of the increased frequency of the lung as a site of cancer, by taking averages of figures prior to 1910 and subsequent to 1920. Most of these quotations have been verified. Various other records, less complete, or representing periods unsuitable for comparison, have been included in Table II. Table III, modified from a combination of results published by Bonser, shows the clinical and post-mortem findings and is briefly commented upon.

From Table I it will be seen that figures obtained from three Continental authorities show no marked increase, their earlier figures corresponding to those of other observers while the latter figures are much lower. The lack of increase as shown by Bonser has already been mentioned. A study of these tables will readily indicate that, where a considerable number of cases has been examined post-mortem, the figures are in close agreement. Where autopsies have been few the results are less significant owing to greater range of error.

TABLE IV. CANCER OF LUNG.

Author.	Total number of cases.	Average Age.	Age Incidence in decades. Total number of cases	-30	30-40	40-50	50-60	60-
Shennan	22	50 4/12	16		3	4	6	3
(1) Duguid	175	45½	173	20	31	40	50	12
(2) Bonser	170	50	170	17	35	39	46	33
Weller	14	50⅛	14		1	6	5	2
Hunt	26	48¾	26	1	5	8	9	3
Miller and Jones	32	51½	32	2	2	13	10	5
Eloesser	(27)		21		1	4	10	6
Barron	13	54¼	13			5	5	3
Kikuth	(246)		246	7	18	49	77	95
Grove and Kramer	24	50	24	1	5	7	6	5
Simpson	139	48	139	10	18	41	45	25
Davidson	107	50	107	8	20	41	30	6
Fried	12	53¾						
von Gahn	6	60⅓						
Vinsen, Moersch and Kirklin.	77	49½						
Maxwell	184	46½						
Frommel	41	58						
Crohn and Weber	11	50						
	1043	51	981	65	139	257	300	198

(1) "175 intrathoracic neoplasms" excluding "invading lymphadenoma". Of 78 examined histologically 68 were definite bronchial carcinoma and 10 were "doubtful".

(2) 22 cases "involved mediastinum only" and 52 of 60 cases examined histologically were carcinoma of lung.

AGE AND SEX INCIDENCE.

With regard to age and sex the statistics are sufficiently beyond dispute to require much explanation. In the corresponding tables the figures concern almost entirely cases of primary carcinoma of the lung diagnosed at autopsy. It has not been thought necessary to consider periodic changes and fluctuations. Most of the examples quoted are of recent date, and it would not be possible to indicate accurately any changes in age incidence or sex ratio which may have taken place. From his own experience, Davidson believes that he is now dealing with younger sufferers from lung cancer than was formerly the case.

In the Tables IV and V the series grouped together are those of individual observers except in that of Kikuth which contains examples from other Continental writers, whose figures have not been included however in any of the other results quoted. A considerable number of cases have been collected and arranged in decades. Of the other groups, wherever possible the average age has been calculated. Barnard has mentioned that the "oat-celled" tumours would appear to occur at an earlier age than the other pathological varieties, the "oat-celled" growths occurring between the ages twenty-seven and sixty-six and the remainder of his series from forty-four to sixty-one.

The/

TABLE V. CANCER OF LUNG.

SEX INCIDENCE.

Author.	Total number of cases.	Male.	Female.
Shennan	18	15	3
(1) Duguid	175	151	24
(2) Bonser	170	132	38
Fried	12	9	3
von Gahn	6	5	1
Hunt	26	20	6
Parish	32	28	4
Vinsen, Moersch and Kirklin	29	23	6
Barron	13	10	3
Eloesser	25	23	2
Grove and Kramer	24	22	2
Maxwell	184	140	44
Beal	15	10	5
Kikuth	246	159	87
Weller	14	13	1
Simpson	139	111	28
Davidson	107	89	18
Miller and Jones	32	24	8
Strada	17	16	1
Frommel	41	30	11
Crohn and Weber	11	10	1
Marsman	15	14	1
Rist and Rolland	23	16	7
	1374	1070	304
		77.87%	22.13%

(1) & (2) See footnotes of Table IV.

The occurrence of cancer of the lung has been recorded in a girl aged sixteen months, in whom Schwyter found adenocarcinoma of almost the whole left lung, while Frommel has reported its occurrence at the age of ninety-one. It will be seen that the majority of the cases are evident in the fifth and sixth decades.

As regards sex incidence, there is a marked male preponderance. Apart from the series which have been collected, Kikuth gave a male - female ratio of 1.9 : 1, Sachs as 1.8 : 1, and Biberfeld found the proportion to be 2.9 males to each female. These figures correspond to less recent periods.

From Table IV it will be seen that of 1,043 cases of pulmonary cancer the mean of the average ages was fifty-one years, and of 981 cases which could be grouped in decades, 300 occurred between the ages of 50 and 60, and 557 between the years 40 and 60.

From Table V denoting the sex incidence, the males formed 1070 (77.87%) and the females 304 (22.13%) of the total 1374 cases, indicating a male to female ratio of $3\frac{1}{2}$ to 1.

OCCUPATION.

While the question of occupation will assume importance as an aetiological factor of pulmonary cancer the established facts may be mentioned at this stage.

Duguid/

Duguid traced the occupation in 143 of his male cases of whom 29 were labourers, 9 carters and 8 were clerks. Reviewing his series of 175 cases, and taking into consideration the fact that at least three quarters of the adult population of Manchester were in-door workers, he found that the incidence in the latter was only one third as great as that of the out-door workers. Hudson found cancer of the lung to be more common in grooms and stablemen. This finding has not been confirmed. Bonser of Leeds, studying 107 cases whose employment was known, met with no occupational predisposition and found the incidence to be approximately equal in those following indoor pursuits and out-door workers. Davidson could recognise no predisposing influence connected with occupation in the Brompton Hospital series.

Frommel and others maintain that workers exposed to mineral or vegetable dust (as were 22 out of 29 of this author's examples) are more susceptible to cancer of the lung. The much quoted prevelance of cancer in the Schneeberg Miners would seem to have justified this statement and will be discussed more fully under the predisposing factors.

PREDISPOSING FACTORS.

While factors which are said to predispose to malignant growth generally must be evident in the bronchi and lungs, specific features, which add to the interest in the development of cancer, are present in this situation. An organ commonly infected by tuberculosis, prone to other infections of varying severity and of prolonged nature, subject to the inhalation of irritating gases and particles of all descriptions, the lung offers its tissues as a sacrifice to cancer growth on lines which have provided scope for many theories. The most striking of the facts which can be adduced will be detailed and an endeavour will be made to summarise the more important of the theories advanced by different observers.

Trauma has been considered a factor by some writers, of whom Maxwell and Nicholson quote Autrecht and a report by Georgi in 1879. A few isolated instances are available where there has seemed to be some relation between injury and malignancy. It would appear that these associations were co-incidental.

Ewing states that the chief aetiological factor in carcinoma of the lung is tuberculosis. As this disease is almost universal and as the majority of individuals/

individuals show tuberculous lesions in the mediastinal glands, and a considerable number have healed foci of infection in the lungs, it seems unlikely that any close association should be formed between the two conditions. While several cases are recorded where carcinoma has occurred within a tuberculous cavity such coincidence is relatively rare. Grove and Kramer found associated tuberculosis in 2 out of 24 cases of lung cancer. Shennan has recorded the growth of a squamous carcinoma in relation to an old tuberculous lesion. With the exception of one instance where the other lung was tuberculous none of 21 other cases showed this association. Friedlander reports the occurrence of carcinoma in the wall of a tuberculous cavity. Adler found tuberculosis in 19 of 374 cases, while Maxwell and Nicholson recorded the association of both lesions in 12% of lung cancer. It is unnecessary to quote a large series of figures as it will be seen from those already given that cancer and tuberculosis do occur in association with one another not infrequently but that the coexistence is not very striking. Numerically in fact, from the assumption that tuberculosis is a fairly common finding in the form of healed foci within the lungs in a great proportion of cases examined post-mortem it would seem that the association is placed unexpectedly low.

Syphilis has been mentioned by some writers and

Smith/

Smith found the Wassermann reaction to be positive in six of twenty-seven cases (27%) of pulmonary carcinoma. There are few definite facts or figures worthy of further consideration.

Influenza has been cited as a predisposing factor in the development of lung cancer. The high incidence at special periods has been attributed to epidemics of influenza during the previous years. Shennan suggests that the increase in incidence during 1924 was the result of chronic interstitial pneumonia which remained as a legacy of the influenza epidemics of 1918 and 1920. Nine out of twenty-two of his cases showed chronic interstitial pneumonia. Barron discusses the work of Askanazy, who demonstrated the replacement of the ciliated epithelium of the trachea and bronchi by squamous cells in 38 of 90 cases which died during the influenza epidemic of 1918. The effects of influenza, occurring equally in both sexes, have caused no alteration in the sex incidence of lung cancer and it is difficult to correlate the two diseases closely though there may be some indirect relationship.

Many patients present a history of previous influenza acquired sporadically or during epidemics. In some it is possible to consider the illness as the first manifestation of new growth which may have caused slight/

slight fever in virtue of its local extension or of its secondary effects. The increase in incidence of lung cancer has been shown to be a gradual one and the figures, generally speaking, do not indicate the fluctuation or sudden rise which would be consequent of a direct relationship between the epidemics and malignant growth. Kerley has pointed out that in Iceland no cases of pulmonary cancer have been reported while the ravages of influenza have been exceptionally severe. As Adami has shown, influenzal catarrh tends to be specially localised to the lower end of the trachea and to the main bronchi in such a way as to encourage the invasion of streptococci and pneumococci and so to produce interstitial pneumonia. Together with the work of Askanazy on the epithelial changes these facts may indicate a condition produced by influenza which may be considered favourable for the development of malignancy. It is unwarrantable that any closer relation be alleged.

The question of the association of cancer with mechanical irritation naturally follows. While there has been no obvious occupational factor except in the case of the Saxon miners, the influence of irritation due to street dust, petrol fumes, coal dust, tar particles, silica, metallic dust, and other substances as a direct or an indirect factor in the production of lung/

lung cancer has been the subject of much discussion.

Experimental work has been undertaken by Kimura, Winternitz, and others. Kimura was said to be able to produce lung cancer in rabbits by the intratracheal insufflation of tar. Kikuth quotes Winternitz who showed a similar result in the bronchi of animals by means of cauterisation with hydrochloric acid. Murphy and Sturm recorded the production of primary lung cancer in 66% of mice by painting the skin with tar. By means of an ingenious device Smith made similar experiments with tar fumes and gasolene but he was unable to confirm the results obtained by the previous workers. It is not generally agreed that the lesions which experimental irritation has produced and which are stated to have been malignant are virtually neoplastic. It is probable that confusion may have arisen between the appearances of inflammatory reaction and of new growth.

The clinical aspect of the development of carcinoma of the lung is exemplified by the investigations of the cases occurring in the Schneeberg miners. This example has been quoted in most of the writings on this subject and deserves mention here. In these mines in Saxony, the dust contains iron, bismuth, tin, zinc, lead, manganese, uranium, cobalt, and nickel, chiefly in combination with sulphur and arsenic (nearly .5% at times), and 50 Meché units of radio-active emanations/

emanations. Duguid quotes Arnstein who stated that one third of all the miners admitted to hospital from 1907 to 1911 were said to be suffering from pulmonary cancer. The Saxon Cancer Commission investigated 154 cases. Twenty-one died during three and a quarter years during which they were under observation, and in thirteen (65%) of these carcinoma of the lung was demonstrated at autopsy. Old or active tuberculosis was found to be present in seven cases, one of which showed cancer. In the non-mining population of this district the incidence of tuberculosis was higher and there was no prevalence of lung cancer. The clinical features have remained the same for several centuries and are characterised by a preliminary stage lasting for some years during which there is chronic cough and debility, followed by a period of shorter duration with the onset of more severe symptoms. The early stage has been referred to pneumokoniosis and the later exacerbation to the onset of malignant disease. This sequence has been confirmed by radiological evidence.

Davidson quotes information from Levy Simpson who found an unduly high incidence of lung cancer amongst the radium miners of Czecho Slovakia. It has not been possible to find in the literature any other evidence to support the suggestion that radium emana-

tions/

emanations take a place of prominence as a factor predisposing to cancer of the lung.

The contrast between the associations of silicosis and tuberculosis in Saxony and in South Africa is of interest. In the former country tuberculosis is relatively rare while in Africa tuberculosis is the commonest complication of silicosis. On the other hand the figures from the South African mines, according to Simpson, show that in 1924-1926 only two cases of lung carcinoma were found co-existing with and in only five cases occurring apart from silicosis. The presumption would appear to follow that silicosis is not in itself a vital factor in predisposition to lung cancer, and that the prevalence of lung cancer in Schneeberg must be due to other reasons.

In the literature dealing with asbestosis and silicosis there is little mention made of any association between these conditions and malignant growth. So far as can be ascertained, at least in this country, chemical agents have not proved to be predisposing factors. Kikuth has reported the case of a chemist who developed carcinoma of the lung and died fourteen months after taking employment which subjected him to the inhalation of chlorethylene and chlorethane vapours. This incident is of interest but was apparently an exceptional case.

The increasing incidence of lung cancer has been associated with the use of tar in road-making and with the inhalation of petrol fumes from motor cars. Tobacco has also been cited as a possible factor. In considering these substances we have constantly before us the inexplicable fact of the preponderance of males in the sex incidence of pulmonary cancer. While the female sex tends to lead an in-door existence the situation is complicated by the evidence of several authorities that, amongst the males, indoor and out-door workers have shown the same incidence of the disease. Whether there is some accessory factor determining cell-growth in the female, or whether the lower incidence among women is due in any way to difference in chest expansion or to the mode of breathing, the explanation of the difference in sex ratio remains unsolved.

Maxwell found old dense pleural adhesions in 105 of 184 cases of lung cancer. He suggests that these antecedent inflammatory changes may limit movement of that side of the chest in such a way that any irritation may be concentrated on that side. It is difficult to assess the value of this suggestion. On the one hand, irritation due to retained secretion would be increased by lack of movement. On the other hand, diminished movement would lessen the irritation due to inhaled material.

At the present time it is almost generally acknowledged that the process of metaplasia, brought about by chronic irritation or by other influences, may be a precursor of malignant growth, especially where the factors continue to exert their influence on the tissues. These metaplastic changes have been seen in the bronchi and lung, and the mode of the process has been indicated. A noteworthy feature is that the increase of incidence of lung cancer, not amongst people of special occupations or exposed to selective factors but throughout a wide range of individuals, has taken place during a period which has experienced the increase of air pollution by various gases and particles resulting from modern factories, roads, and transport. While experimental work has given little definite information, further detailed statistics during the future years may help to decide which, if any, of these factors is most responsible and in what manner the effect can have been so marked on the male sex.

PATHOLOGY.

During the last three decades cancer of the lung has come into prominence by virtue of its increasing incidence, by the new lights which have been shed on its histology, and by the clearer understanding of much of the pathology which hitherto presented disputable/

disputable problems. Amongst the contributors in this country Shennan and Barnard have done much to clarify the histological details, the latter paying special attention to the so-called "oat-celled" tumours. Duguid has recently published a series of cases with accurate histological details, and still later Simpson and Hunt have added valuable studies.

Pathological opinion has shown great changes from the time of Virchow and his contemporaries down to the present day. Increased knowledge of cytology and improvements in the use and interpretation of staining reactions have reorganised the lines of thought to a marked extent. Many cases originally diagnosed as mediastinal lymphosarcoma are now regarded as epithelial tumours of the "oat-cell" type originating in the bronchi. In the classical work of Adler published in 1911 the collection included 374 carcinomata and 90 sarcomata. These figures would now doubtless be modified in the light of more recent pathological opinion.

SITE./

TABLE VI. CARCINOMA OF LUNG. SITE OF GROWTH.

Author	Total No. of cases	Right lung.	Left lung.	Media-stinum.	Both lungs.
Shennan	21	15	4	1	1
Duguid	175	78	67	12	18
Bonser	172	65	57	22	28
Fried	11	4	7		
Hunt	26	16	10		
Parish	32	19	13		
Vinsen Moersch and Kirklin	29	20	8	1*	
von Gahn	6	2	4		
Barron	13	5	8		
Eloesser	23	7	16		
Playfair and Wakeley	4		4		
Grove and Kramer	21	5	12	1*	3
Maxwell	184	93	90	1*	
Beal	14	4	10		
Simpson	139	69	70		
Davidson	107	59	36	12	
Kikuth	246	123	118		5
Weller	13	6	7		
Miller and Jones	32	21	11		
Total	1268	611 48.2%	552 43.5%	50 4%	55 4.3%
McCrae et al.	202	40.0%	47.0%		9.0%
Heuer et al.	662	48.4%	46.8%		4.8%
* Brunn (series)	626	283(46.5%)	246(40.9%)		26 (4.3%)

* Adler, Cathin, Lavinovitch, Rusk, Eloesser, Carmen, Barron etc.)

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SITE.

In the view of many observers the right lung is a more frequent site of carcinoma than the left, and the upper lobes are said to be more favoured than the lower lobes. Hunt quotes Seyfarth who found the right lung to be affected twice as often as the left lung, with whom Holzer, Briese, and Wolf concur. An attempt has been made to reach as accurate a conclusion as possible by tabulating the figures from the records. The results are not within strict bounds of accuracy as the reports have come from many sources, many of the carcinoma being grouped as occurring in the mediastinum and others being omitted as doubtful. In most cases this is taken to infer involvement of the mediastinum so that origin from one particular lung or lobe cannot be correctly stated. Where details have been given the cases have been grouped in a further table. Here fallacies are still more difficult to avoid as accurate localisation of the site of origin is impossible in many specimens of pulmonary neoplasm. Table VI shows the site of growth in 1275 examples of cancer of the lung to be on the right side in 611 (48.2%), on the left in 542 (43.3%), both lungs being affected without obvious origin from either side in 55 (4.4%) and the growth recorded as involving the mediastinum only in 60 (4.8%) cases, including 3 in which/

TABLE VII.

Author	Total No. of cases	Right							Left			
		Main Bronchus	Upper lobe	Middle lobe	Lower lobe	Upper & middle Ls.	Middle & lower Ls.	Whole lung.	Main bronchus	Upper lobe	Lower lobe	Both lobes.
Shennan	18	6	3		4		2		1	1	1	
von Gahn	6	2							2	1	1	
Maxwell	183	54	21	2	16				59	15	16	
Kikuth	240				35	38	49			31	30	57
Weller	13	5	1						3	1	3	
Miller & Jones	32	8	5	1	6			1	3	3	4	1
Fried	11	3						1	3	1	3	
Total	503	78 15.5%	30 5.8%	3 .58%	61 12%	38 7%	51 10%	2 .4%	71 14%	53 10.5%	58 11.5%	58 11.5%

which cancer had arisen in the trachea. Other series may be quoted for purposes of comparison. Of 662 cases collected by Heuer, Andrus, and Taylor, 321 (48.4%) occurred on the right, 310 (46.8%) on the left side, and 31 (4.8%) affected both lungs. Brunn's series of 626 cases which included 374 recorded by Adler, those of Eloesser and Barron given in Table VI and others, showed the right side to be affected in 283 (46.5%), the left in 246 (40.9%), and both lungs in 26 (4.3%). Finally a third independent series of 202 cases is recorded by McCrae, Funk, and Jackson (including 90 reported by Weller and others by Passler), 74 (40%) originating in the right, 89 (48%) in left side, and 17 (9%) affecting both sides. These figures are in fairly close agreement with the exception of the last series where there is a preference for the left side.

The conclusion may be made that cancer of the lung affects the right and the left lung with almost equal frequency. Table VII requires little comment. As it has been stated the figures are not entirely comparable in view of individual variance in the determination of localisation. Of 503 cases, the growth appeared to have originated in the right and left main bronchi in 15.5% and 14% respectively. From the other results/

results the feature of special note is the apparent rarity of incidence in the right upper lobe alone. Kikuth's figures, which greatly influence the conclusions, are obviously recorded on a basis different from the others. Taking those of Maxwell as representative, it will be seen that there is little difference between the figures either for the two sides or for the respective lobes. Of the total 503 cases recorded in this table 253 occurred on the right and 240 on the left side.

While it has been possible to determine the origin of the growth as regards site in many cases of lung cancer, in advanced lesions it is frequently extremely difficult for localisation of origin to be accurately discovered. It is generally agreed however, from bronchoscopic inspection and from examination of post-mortem specimens, that the commonest point of origin lies a short distance below the point of bifurcation of a main bronchus in the region of the commencement of the minor bronchi. The angle formed by the epi-arterial and the main bronchus is a favoured situation for the development of carcinoma.

MORBID ANATOMY.

Formerly the knowledge of morbid anatomy depended almost entirely on post-mortem verification for a correct appreciation. It is now possible to examine during life many lung tumours by bronchoscopy, and indirectly by means of radioscopy. McCrae, Funk, and Chevalier Jackson have recorded their experiences in the study of intrabronchial tumours by means of the bronchoscope. These workers described the endobronchial growths as nodular or sessile, sometimes pedunculated and fungating. The nodules may be single or multiple, red or yellow in colour with unusually large blood vessels, and often obliterating the normal appearance of the bronchial rings. Absence of normal rhythmical movement indicates fixation of the tissues. The mucosa proximal to the growth commonly shows longitudinal ridging. These appearances are modified by ulceration, bronchiectasis or abscess formation. Rarely carcinoma of the bronchus is evident as a superficial mossy growth spreading on the surface of the mucous membrane, and occasionally the tumour is seen as a single nodule or as a ring of nodules causing stenosis of the bronchus.

In post-mortem specimens the typical appearance is that of a whitish grey mass at the hilum with white cords/

cords of solid tissue radiating along the bronchi towards the periphery. The growth may be present as a localised mass, usually at the root and sometimes having the appearance of encapsulation.
A single lobe may be consolidated by malignant growth, the interlobar septa appearing to act as a barrier and the remaining lobes being healthy. The growth may be situated at the periphery as a white mass with an irregular margin and showing a tendency to spread along the lines of the bronchi towards the root. In such a case careful examination of the larger bronchi may lead to the discovery of a small tumour from which the main mass may have originated. Less commonly the neoplasm is situated in the mediastinum, spreading to both lungs, or showing little apparent involvement of either lung. Affection of one lung alone may occur as a massive malignant consolidation or in the manner of a lymphangitis, the whole lung being studded with miliary nodules. The latter is the rarest of all forms.

Miller and Jones formed a careful survey of 808 cases of carcinoma of the lung. They placed these cases in ten groups and studied the symptoms associated with each of these types:-

(1) Intrabronchial growth tending to blockage of the lumen.

(2)/

(2) Peribronchial tumours affecting the lining epithelium and spreading along the bronchi producing a growth radiating from the root.
(3) Solitary nodules at the periphery or at the hilum.
(4) Schirrous type in the parenchyma of the lung with infiltration of a lobe - a rare form.
(5) Mediastinal growth.
(6) Massive consolidation with infiltration of part or of the whole of a lobe.
(7) Massive consolidation with abscess formation.
(8) Bronchial obstruction due to growth with consequent bronchiectasis, abscess, and pleural effusion.
(9) Patchy infiltration with discrete nodules.
(10) Miliary carcinosis - extremely rare.

Maxwell has placed his series of 184 cases of primary lung cancer in four groups. Type I is composed of 15 cases localised and without infiltration. Type II has 49 examples of growth with surrounding spread by direct extension, by the lymphatics, or by both means. In Type III, 36 cases, spread is chiefly to the mediastinum. Type IV is the largest and is composed of 84 cases showing infiltration of the lung and of the mediastinum. This classification is more condensed than that given by Miller and Jones and appears to be based on the general appearances.

Cancer growth may assume so many unexpected forms that/

that it is difficult to give a dogmatic opinion of the histological type of any specific gross form. It is therefore sufficient to consider the details of only the more common types as to their local and general behaviour. Later the histological study may enable some association to be made between the individual cell types and the appearances presented by and the behaviour of the tumour. It is extremely difficult to form an accurate estimation of the frequency with which these different gross types occur as they are seen at various stages of growth and extension, and the appearances are so commonly modified by the secondary changes, atelectasis local or massive, bronchiectasis, and infective processes both within the tumour and within the lung. At the beginning of this section the gross appearances presented by the various types were mentioned more or less in the order of their frequency.

In a broad sense these growths may be thought of in two main groups: those of an obstructive type closing the lumen of the bronchus by growth within or by pressure from without the bronchial wall; and a second group comprising the other tumours which tend to form a cancerous mass without definite direct obstructive results. This conception may be helpful chiefly in the consideration of the secondary effects which/

which so often mask the primary pathological and consequently the clinical pictures.

When stenosis of a bronchus is present the distal lung tissue may be collapsed. The area affected depends on the bronchus involved, blockage of the lumen of a minor bronchus producing lobar collapse and massive atelectasis occurring as the result of complete stenosis of the main bronchus. Coryllos has indicated the modes by which collapse of lung tissue may occur and the relation of super-added infection or underlying infection to the lesion produced as the final result. Simple collapse has been seen to occur as a result of bronchial obstruction by some of the intrabronchial benign growths. The same process may be evident with malignant tumours but, as in the benign forms, infection is more often associated and abscess or bronchiectasis is produced. The latter may be of either cylindrical or saccular types.

In the series of 184 cases of lung cancer described by Maxwell, bronchiectasis was present in 65 and lung abscess in 38 cases. In Simpson's series of 139 cases there was bronchial occlusion in 78, of which bronchiectasis and bronchopneumonia were found in the majority and lung abscess in 16 instances. Pleural effusion is present at an early stage in some, and eventually in more than a third of cases and, according

to/

to Fishberg is commoner with tumours of the lower lobe. Empyema occasionally follows a sterile effusion or it may occur secondarily after the rupture of an abscess or as a result of infection from a tumour. The growth itself may show necrosis and cavitation. Spontaneous pneumothorax is extremely rare. Erosion of vessels has produced small aneurysms from rupture of which fatal haemorrhage has occurred.

MODE OF SPREAD.

A study of the gross anatomical features of tumour growth within the lung has given evidence of the methods by which spread may occur. These may be dealt with simply in terms of local and distant extension.

Local extension may occur along the surface of the mucosa. This rare method was noted in the case of Letulle and Jacquelin where cancer of one bronchus was seen to spread over the surface of the tracheal bifurcation so as to involve the main bronchus of the opposite side. Extension is found more commonly in a peripheral direction with replacement of the bronchial epithelium by tumour cells along the lines of the bronchial tree. Many cases showing this phenomenon have been noted, that of Davidson and Ledlie forming

an excellent example in which no pulmonary growth was evident until the bronchi were opened. Similarly spread may occur round the circumference and produce obstruction of the lumen. Langhans described a case with a ring-like constriction due to a tumour arising in the mucous glands, the surface epithelium being intact. Extension also occurs into the parenchyma of the lung and thence to the surrounding tissues, the pleura, and mediastinum. The interlobar and interlobular septa tend to delineate the growth and the alveolar walls are used as supporting stroma. The presence of papillary projections into the alveoli will be explained in the description of the histological appearances. Mediastinal involvement affects the pericardium in most cases, less commonly the heart, the oesophagus, and the vena cava. The vertebrae and ribs may be eroded by direct extension or by metastasis. The aorta is infiltrated rarely and the pulmonary artery may be involved. The recurrent laryngeal nerves, the vagus and phrenic nerves may be affected, and paralysis of the vocal cords or of diaphragm is not uncommon. It has been found that the nerves are affected by pressure rather than by infiltration.

In Maxwell's series of 184 cases, the superior vena cava was infiltrated in 25, the left innominate vein in 4, the heart and pericardium in 40, the oesophagus/

oesophagus in 25, the aorta in 20 and the pulmonary artery in 14 instances, and nerve involvement affected the recurrent laryngeal nerves in 14, the right phrenic in 2 cases and the left vagus in one case.

Simpson gives similar figures. Of 139 examples of lung cancer the pericardium was invaded in 62 and the oesophagus in 17 cases. While invasion and obstruction of the superior vena cava occurred in 16 instances, the inferior vena cava was only involved in one case. Thrombosis was found in 24 of this series and affected the venae cavae, innominate, jugular, maxillary, iliac and femoral veins.

The lymph vascular system is a common route along which malignant disease is conveyed either as emboli or by permeation. Before dealing with this mode of spread brief mention may be made of the lymphatic system of the lung. Scott and Beattie have made a careful study of the lymph glands and vessels associated with the lungs and pleurae of the higher apes. Their work is valuable on grounds of comparative anatomy. These observers found the two plexi of the system to have an independant existence. The superficial plexus lies in the wide meshes of the areolar tissue immediately under the visceral pleura from which the vessels converge to the para-tracheal glands, a few running to the tracheo-bronchial glands. The deep plexus/

plexus has vessels passing along the bronchi and bronchioli to the parenchyma connecting all the small lymph nodes, the terminal vessels ending 4-5 millimetres short of the superficial plexus. The fine submucous plexi in the bronchi communicate with the deep plexus. Injection of this system has shown no evidence of its existence in the alveolar walls. The deep plexus drains lymph into the tracheobronchial glands, whence vessels join those from the mediastinal glands to form the main broncho-mediastinal trunks.

The radiating processes described in the gross pathology as spreading from a growth at the hilum are usually indicative of extension along the peribronchial lymphatic vessels, while the rare condition of miliary carcinomatosis, to which Briese drew attention in 1920, is said to be the result of a generalised carcinomatous lymphangitis. The discovery of an isolated peripheral nodule suggests that spread may have occurred along the lymphatic vessels or by way of the blood stream. In the majority of cases of lung cancer the regional lymph nodes are involved, and in those cases of carcinoma which have appeared to affect only the mediastinum further examination has often revealed a small primary growth in one of the bronchi. In a definite small proportion of cases there is no apparent spread to the hilar glands, and in about one third of growths showing metastasis/

metastasis the distant lymph nodes, within or without the thorax, are affected. In many cases there is evidence of lymphatic spread to the pericardium though the latter is more often involved by direct extension. The example, described by Robertson and already quoted, of an endothelioma-like tumour of the pericardium later proved to be a metastatic growth from a primary bronchial carcinoma appears to illustrate dissemination by means of the lymph vessels. The pleura may be affected by direct extension or by spread in a retrograde path along the lymph vessels, and this involvement is usually followed by pleural effusion. Extension more remotely to the liver or to the thoracic wall may also occur by these means.

Grove and Kramer quote Moise who believes that spread may occur by gravity and by aspiration as well as by the more generally recognised means. Such cases must be extremely rare and the process would seem to be due to the passage down the bronchi of portions of tissue separated from the surface of an ulcerated tumour. Such pieces of malignant tissue are occasionally evident in the sputum. This method of extension is obviously less common and of little importance.

The blood stream affords a ready means by which portions of malignant tissue may be dispersed. Ulceration/

TABLE VIII. CARCINOMA OF LUNG. METASTASES

Author	Total No. of cases noted.	Extra thoracic Lymph nodes.	Liver	Kidney	Supra-renal.	Bone	Brain	Spinal Cord.	Spleen	Thyroid	Pancreas	No extra thoracic meta-stases.
Rist & Rolland	11		5	2	1	2	2		1			
Shennan	10	5	4				3	1				2
Duguid	78	26	27	9	18	8	2		1			
Playfair & Wakeley	4			1	3							
Bonser	172	38	43	27	26	7	7		3	1	15	
Barron	13	9	4	5	4	4	2		2			
Eloesser	27	5	6	5		1			1			
Grove & Kramer	24	6	12	8	5	8*	5		2	1	4	
Maxwell	184	86	60	29	32	8	16+		5	4	21	14
Simpson	139	70	45	14	41	85	19	1	5	4	25	
Kikuth	246		70	25	21	48	31		2		11	
Weller	12	4	6	1	1	4	1		1		1	2
Miller & Jones	808 series	-	30.7%	15%	9.7%	11%	9.5%		.8%	1%	1.4%	
x Brunn	626 series		30%	20%	14%		12%					
Total	920	249 27%	282 30%	126 13.7%	142 15.5%	175 19%	90 10%	2	23 2.5%	10 1%	77 8.3%	18 2%

Note:- The percentages given are based on the number of cases in which the organ is involved of the total number of the series in which the specific organ appeared to be examined. Avoidance of fallacy with regard to certain organs is obviously difficult.

x Including cases of Adler, Cathin, Lavinovitch, Rusk, Eloesser, Carmen and Barron.

* Bones - Ribs 5; Calvarium 2; vertebra 1; zygoma 1; ilium 2; neck of femur 1; occipital bone 1; sphenoid 1. Pathological fractures 3.

Ulceration into a radicle of a pulmonary vein may scatter malignant emboli to distant organs, or neoplastic cells may reach the right auricle by way of the broncho-mediastinal trunks and metastatic nodules may be produced in the lungs. By the latter means as well as by retrograde lymphatic spread, the opposite lung or other parts of the same lung may be affected. Spread by the blood stream may occur at any stage in the course of the process. Dissemination of emboli may result in few or multiple metastases. The lymph vascular system plays a greater part in the extension of pulmonary carcinoma, as in most other epithelial tumours, especially in the earlier stages of growth.

Metastasis in distant organs may be dealt with briefly. A table of the records has been compiled in order to give a somewhat rough estimate of the relative frequency with which secondary growths are found in the various organs. In the observations recorded in Table VIII there are many fallacies owing to the differences in routine examination and to the degrees of accuracy employed by various workers. Some authorities have not made a study of the brain with regard to secondary growths, and in the same way many metastases in bones will have been overlooked. In view of these fallacies the percentage figures given must indicate/

indicate the minimum occurrence of metastases in each organ. The organs most prone to error of notation are the lymph glands (Kikuth has not included extra-thoracic glands in his reports), the brain, the bones, the thyroid and the spinal cord. The other organs are usually examined and the corresponding figures may be taken as reasonably accurate. Of 920 cases of lung cancer where metastasis has been recorded the following figures are comparable:- Liver 30%, Bones 19%, Supra-renal 15.5%, Kidney 13.7%, Brain 10%, Pancreas 8.3%, Spleen 2.5%, Thyroid 1%. The spinal cord was the site of metastasis in two cases of this series. For purposes of comparison the collections of cases by Brunn, and the series recorded by Miller and Jones are added.

The liver is the commonest site of secondary growth and is probably involved usually by way of the blood stream, and more rarely by lymph vessels through the diaphragm or from the coeliac glands. Direct extension to the liver is unusual.

The skeletal system is involved in 19% of the compiled series. As has been shown the bones are often overlooked during autopsy and the figure given must therefore be regarded as a minimum. Bone is thus a favoured site of metastasis from pulmonary cancer. Simpson has noted involvement of bones in 85 of his series of 139 cases. The individual bones were:-

vertebrae/

vertebrae 29, femur 21, ribs 15, sternum 8, skull 5, pelvic bones 4, humerus 2, clavicle 1. These secondary growths are due chiefly to spread by the blood stream though the vertebrae may be affected by retrograde dissemination through the lymph channels.

The suprarenal glands are a comparatively common site for metastasis, which is presumably blood-borne, and it is difficult to account for the frequency with which secondary nodules are found in this situation. Occasionally a suprarenal gland is involved by direct extension from an affected adjacent lymph node.

The kidneys suffer not uncommonly as in other forms of cancer. The heart was involved in 21% of Brunn's series. This organ has already been mentioned with regard to direct extension from the primary tumours. In Weller's opinion the metastases to the heart are usually due to direct extension through the pericardium in the perivascular lymph vessels or along the lumina of the great vessels themselves.

The brain is probably affected more often than is supposed, as it is not always examined at autopsy. The importance of intracranial metastasis lies in the fact that of the organs involved the brain is often the only source to which symptoms are referable. Cerebral metastasis is usually due to dissemination by the blood stream. Miller and Jones quote Hassein who/

who suggested a retrograde ascent along the perineural lymphatics from the neck to the subdural and subarachnoid spaces. Fried and Buckley found metastases in the brain in fifteen of thirty-seven cases of lung cancer, and in eleven of these a diagnosis of primary tumour of the brain had been made. They attribute the involvement to spread by the blood stream by way of the pulmonary vessels. In four of Fried's cases tumours were removed from the brain at operation. Dosquet found metastases in the brain in 33% of 105 cases of lung cancer. Ferguson and Rees point out that where neurological symptoms result from metastatic growths, in the brain they are due to cerebral rather than to cranial deposits, while in the cord they are almost always the result of pressure from metastases in the bone. From a study of the literature the authors have found only eight examples of true medullary deposits. Cornwall examined the meninges and found microscopic evidence of metastasis from carcinoma of the lung. To this Winkelman and Eckel have given the names Pachymeningitis carcinomatosa and meningitis carcinomatosa as the growth affected the dura and the pia mater respectively. In the nine cases described by Ferguson and Rees the cerebral metastases were bilateral in three and situated on the right side in three cases, while the left side alone was affected in one case. The cerebellum is occasionally involved by/

by metastasis.

Secondary growths are recorded in the pancreas in 8.3% of the cases in this collection. It seems probable that in many instances the gland may become involved as a result of retrograde spread from the para-aortic lymph glands which are commonly affected. It is not unusual to find malignant enlargement of a lymph nodule in close proximity to the head of the pancreas and occasionally growth has extended to the latter. Spread by the blood stream may also occur and several nodules may be scattered throughout the gland, presumably by this means.

Extra-thoracic lymph glands are involved in 27% of this series of lung cancer. Here again is an instance where the figure must represent the minimum. The supraclavicular glands and the para-aortic chain, especially the coeliac group, are most commonly affected. Glands related to the pancreas, kidneys, suprarenals, and the lower deep cervical groups are frequent sites of metastasis. Other lymph nodes which may be involved include the mesenteric, iliac, and rarely the axillary and infra-clavicular glands. Extension to the various stations of the lymph vascular system mentioned does not differ from the customary progress of malignant growths and requires no special discussion.

Metastases have been found in the ovary, prostate, stomach,/

stomach, gall bladder, intestine, urinary bladder, uterus, parotid gland, eye, muscle, skin, and other tissues.

Finally it may be emphasised that these records are based on post-mortem evidence and that the statements with regard to metastases refer to cases which have died as a direct or indirect result of pulmonary cancer. It is in no wise to be inferred that carcinoma of the lung gives rise to secondary growths with any greater degree of readiness than do malignant neoplasms in other situations. From a correlation of the pathological features with the clinical course the converse might be suggested. Indeed it would appear remarkable that generalised extension should not occur earlier from so active and so vascular an organ as the lung.

HISTOLOGICAL FEATURES.

The histogenesis of pulmonary carcinoma has given rise to much controversy. Ewing recognises three groups of tumours arising from (1) bronchial epithelium, (2) Bronchial mucous glands, and (3) alveolar epithelium. While there is general agreement about the existence of the first two groups the origin of lung cancer from alveolar epithelium has been debated and much has been written on this subject. As has been/

been mentioned above there is always a tendency to associate the site of a tumour with its origin and, in this instance, tumours arising in "the parenchyma of the lung" are often said to have originated from alveolar epithelium. Ewing says that "in the pulmonary parenchyma it is difficult to distinguish the parts played by vesicular and by bronchial epithelium, and in many instances the tumours appear to arise from both sources". It must be remembered that even in the "parenchyma of the lung", a phrase used synonymously with the term "central areas", the smaller bronchi are existent and their cells are capable of malignant transition. Schafer describes the alveolar epithelium as consisting of flattened cells with "here and there groups of smaller and thicker (cubical) epithelium cells". These cells are not generally recognised and their malignant growth may be responsible for some of the tumours whose origin is debated.
It is acknowledged that pulmonary epithelium readily undergoes metaplasia and it is therefore difficult to cite a particular origin to a tumour on the sole grounds of its histological features unless the growth is localised in such a way as to remove doubt. Such certainty of origin as may be demonstrated in growths of the larger bronchi is thus less evident in tumours having a central site. Heuer describes the three histological types in agreement with Ewing, but he sums/

sums up the situation in a philosophical manner worthy of quotation, "However we must be cautious in dogmatically assigning an origin to a given pulmonary carcinoma on the basis of a predominant type of cell since the entire bronchial tree and lungs are the result of outgrowth from the primitive foregut, and in the primordium are composed of a single type of cell. Further modification takes place with the development of the respiratory system but it is entirely conceivable that a carcinoma arising in the alveolar wall might produce an embryonal type of cell closely simulating those of the bronchi". Finally it may be mentioned, as Weller suggests, that it is only now beginning to be understood generally that the type of cell which constitutes the carcinoma is much more indicative of the degree of differentiation than of precise histogenesis.

Before considering the lung tumours on a basis of the various cell types it may be well to describe those growths whose nature appears to be clearly defined. In the larger bronchi carcinomata originating from the lining epithelium are often of a papillary form projecting into the lumina with invading processes spreading along the bronchial walls and along the septa. They are mainly composed of columnar cells showing various degrees of differentiation. A few of these growths are squamous epitheliomata or have squamous cells/

cells in some areas. Prickle cells with intercellular fibrils are occasionally seen, and more rarely, as in von Gahn's case and others, cell nests are evident. Ewing quotes Wolf who found 8 acanthomata among 15 tumours of bronchial origin. Maxwell's series of 111 primary bronchial carcinomata contained 7 instances of squamous epithelioma but careful search usually revealed the presence of columnar cells in these growths. According to Brunn the squamous type is of slower growth. The remaining tumours of this group arising from the lining epithelium are composed for the most part of cylindrical cells. The development of squamous epithelium is said to be due to the process of metaplasia by which the normal cylindrical cells, with or without cilia, have been replaced by the squamous type. Alveolar arrangements and the appearances of adenocarcinoma have been noted but they are more often associated with growths arising from the mucous glands.

The second type of tumour with a fairly clear distinction is that arising from the mucous glands. The latter lie in a loose fibrous tissue deep to the muscle layers of the bronchi and bronchioli. In early cases these growths are confined to the submucous tissues but they may protrude into the lumen and cause stenosis. Infiltration of the parenchyma and ulceration of the surface occur subsequently. The growth is typically/

typically composed of cubical cells in adenomatous arrangement with alveoli of varying regularity. In some instances the alveoli are distended with mucus but this phenomenon is not specially characteristic of mucous gland tumours and may be evident in those derived from other sources.

It has been stated that carcinoma may arise from the epithelium of the pulmonary alveoli which may become filled with columnar or cuboidal cells derived from the walls or may show papillary processes projecting into the lumina. This appearance may however be due to extension of growth from bronchial epithelium into the alveoli.

The more ill defined types of cancer of the lung are the most common and it is this group of tumours which has formed the subject of much debate and controversy. The cells vary considerably in type from columnar, large spheroidal, and polygonal shape to the less distinctive varieties composed of "oat-cells" and small round cells. While the two more clearly defined types originating from the surface epithelium and from the mucous glands may have distinctive appearances there is often no dividing line between these growths and the tumours composed of less differentiated cells. Duguid has classified 68 acknowledged carcinomata in two groups - (1) squamous-cell, which accounted for

13,/

13, and large-cell alveolar types of which there were 16; and (2) oat-cell type - 32, and those composed of small round cells - 7.

In Bonser's series of 60 cases of lung cancer 28 fell to this first group, 24 are of the oat-cell variety, and the remaining 8 are classified as 6 round-cell sarcoma and 2 Hodgkin's sarcoma. Each of the latter eight tumours showed complete similarity between the cells without alveolar formation or transition stages. Shennan separated 25 carcinomata into six groups based partly on cell type and partly on their origin. He has discussed at considerable length the various factors of appearance and staining characterising each type of cell and has emphasised the polymorphism of the columnar, polygonal, and squamous cell types. Barnard, who has provided one of the most valuable contributions, described 19 cases of cancer, of which 7 were obvious carcinomata and 12 were oat-cell tumours. Of the former the appearances varied from the three composed of squamous cells, one of which showed prickle cells and keratinisation, to growths composed of columnar secretory cells. Intermediate varieties were of large polygonal and spheroidal shape and in three of these cases there were associated small oval cells indistinguishable from oat cells. The oat cell group is described with care. These growths consisted of cells arranged in a solid acinar manner,/

manner, oval in shape or round if cut transversely, having little cytoplasm and oval nuclei with a chromatin network which was obscured at times by very deep staining. Other cells, such as large oat shaped, spindle or polygonal cells, could always be found and often there were vague attempts at tubule formation which was definitely seen in one case. This fact is one of the most important features in the diagnosis and classification of these tumours.

Discussing the "mediastinal sarcoma", Barnard notes that "similar tumours do not arise in the lymphatic glands nor in connective tissue elsewhere in the body" and, on the grounds of the characters of the cells, their arrangement, and the stroma, he presents fairly conclusive proof that the so-called oat cell sarcoma of the posterior mediastinum is a medullary carcinoma of the bronchi. Hunt has concurred with this opinion and indicates that the so-called oat cell tumours should be considered as arising "from the bronchial mucosa or from the lung epithelium itself". Eleosser states that the medullary carcinomata and "the lymphosarcomata" show no indication of a bronchial origin and probably originate in the lung parenchyma. Maxwell, on the other hand, describing the histological features of the bronchi, draws attention to a second layer of oat shaped cells lying beneath/

beneath the columnar lining cells - a construction which is not met with in other mucosae, but which is explained by the development of the lung bud from stratified squamous epithelium. He points out that in many of the small-cell growths there was no ulceration, some showing papillomatous outgrowths, and that "it is far more common to find oat cell tumours attempting to form columnar cells than for the columnar-cell tumour to revert to the oat cell type". The findings of this worker agree with those of Barnard in respect of the association of other varieties of cells with those of the preponderating type. He also found that the small cell group usually involved one lung only and gives this fact as an indication of their bronchial origin.

Simpson noted that careful examination of oat cell tumours always revealed areas in which the cells showed definite epithelial characters. Secondary deposits from large cell tubular or from squamous growths were occasionally composed entirely of oat cells. In most of their cases Ferguson and Rees found that the cerebral metastases showed the same type of cell as was present in the primary growth. In one case of primary cuboidal cell carcinoma of the lung, however, the cerebral metastasis evidenced acini and papillomatous characters which were not seen in the primary lung/

TABLE IX. CARCINOMA OF LUNG.

TYPES OF GROWTH IN SERIES EXAMINED HISTOLOGICALLY.

Author	Total	Group I.		Group II.			
		Squamous celled Carcinoma.	Columnar celled large spheroidal Alveolar. Polygonal Papillary adenocarcinoma.	Medullary	Oat celled	Small round celled.	Doubtful.
Shennan	22	5	1	1	2	13	
Duguid	69	13	16		32	7	1
Playfair and Wakeley	4		4				
Bonser	60	7	21		24		8 (1)
Barnard (2)	19	3	4		12		
Hunt	26	2	3		21		
Vinson Moersch and Kirklin (3)	29	16	10	2		1	
Barron	13	2	9	2			
Eloesser	27	11	2	7		2	5
Newcomb	27	2	4		21		
Brunn	2		2				
Weller	14	4	7	3			
von Gahu	6	1	3		2		
Total	318	66 (20.8%)	86 (27%)	15 (4.7%)	114 (35.8%)	23 (7.2%)	14 (4.79%)
Maxwell	111	7	40	64 Group II			
Simpson	138	621 Group I			76		
Total	567	261 (46%)			306 (54%)		

(1) Classified as 6 sarcomata and 2 Hodgkin's sarcoma but conform to small round celled group of Duguid's classification.

(2) Of these 8 in Group I, in three cases small round cells indistinguishable from oat cells were associated and in Group II many cases showed also polygonal cells tubule formation etc.

(3) Diagnosis by tissue removed at bronchoscopy.

lung tumour. The question may be summarised by stating that secondary growths are usually composed of the same type of cell which preponderates in the primary growth of the lung though occasionally the cells may show greater or less differentiation.

Table IX indicates the relative frequency with which the various cell types occur. The arbitrary classification is based on the degrees of differentiation of the cells. In 261 (46%) of the total 567 cases the tumours showed cells mostly of fairly definite structure and arrangement. In 306 (54%) the tumours were composed of less differentiated cells. Of 318 cases the cell types were:- squamous 66,20%; columnar or spheroidal 86,27%; oat cell 114, 35%; "medullary" 4.7%; small round cell 23, 7.2%; doubtful 5%.

An attempt has already been made to correlate the more completely differentiated cell types with the gross appearances, especially in some cases whose origin has been the lining epithelium or the mucous glands. It would appear that in many of these, and in most growths composed of the other types of cell there is little or no relationship between the microscopic features and the gross formation. Similarly there is no special association between any particular variety of cell and the local reaction which it evokes.

Fried/

Fried observes that the rate of growth is inversely proportional to the abundance of metastases. This statement cannot be readily confirmed. In Brunner's experience the squamous epitheliomata showed relatively slow growth and, in the opinion of Schuster and others, the small celled tumours are the most prone to cerebral metastasis.

SARCOMA OF THE LUNG.

It has already been shown that many of the tumours previously designated sarcoma of the lung or of the mediastinum have had their origin from bronchial epithelium. It is possibly due to a swing of the pendulum of opinion in this direction that many authorities now refute the occurrence of primary sarcoma in the lung.

In 1911, Adler recorded 90 sarcomata in his study of the available records, and in 1914 Ross published an account of 60 cases of malignant tumours of the mediastinum, of which 44 were regarded as sarcomata. In many of these the diagnosis would be modified in the terms of modern pathology.

Most observers have employed a classification of pulmonary sarcoma on the basis of size and shape of the cells and the situation of the growth. Ewing enumerates diffuse spindle cell sarcoma, peribronchial sarcoma, large round cell sarcoma, and lymphosarcoma. Many cases diagnosed as sarcoma in these terms have shown characters and arrangements of cells which appear to indicate an epithelial origin, and the behaviour has been so strikingly akin to that of growths possessing a similar appearance whose origin we now realise to be from epithelium that it is difficult to go further than/

than a mere generalisation.

In his discussion of the literature on this subject, Hunt quotes Sonnenfeld who saw only one case of primary sarcoma of the lung, and Newcomb of St Mary's Hospital who found one fibrosarcoma of the lung and one lymphosarcoma of the mediastinum out of thirty intrathoracic cancers. The remainder of the latter series was composed of 21 oat cell, 4 polygonal, and 2 squamous cell carcinoma and one teratoblastoma. Schuster records three sarcomata in a study of sixty cases of intrathoracic cancer, while Shennan includes in his series of 31 cases two examples of sarcoma, one of which he attributes to the thymus and the other to the mediastinal glands. Rosenblum and Gasul have recently reported the occurrence of a primary sarcoma of the lung in a female infant aged 29 months, and they found in the literature records of two other cases in infants and eleven in older children. At a recent discussion on the diagnosis of intrathoracic tumours Melville gave his opinion that the existence of primary sarcoma in the lung was "not proven".

Some of the recorded cases have shown calcification and myxomatous degeneration. Harrington and others have reported instances where benign tumours have shown sarcomatous changes. It seems possible that in many instances there may have been confusion with epithelial tumours/

tumours of similar appearance, especially with the rare type of carcinoma associated with excessive growth of fibrous tissue, and with secondary growths from some distant focus. That sarcoma appears to occur at an earlier age than carcinoma of the lung has been cited as evidence of its entity. Lymphosarcoma originating in the mediastinal glands may spread to the lungs or may possibly have origin in the lymphoid tissue of the lungs. Though this group of malignant intrathoracic tumours is clearly defined its occurrence primarily in the lung is doubtful. Finally confusion in diagnosis may arise in connection with small celled tumours of the thymus which may extend to the lung.

It is unwarrantable to assert that primary sarcoma of the lung does not exist though its occurrence would appear to be extremely rare.

CANCER OF THE LUNG.

SYMPTOMATOLOGY.

The clinical features of lung cancer vary widely according to the type of growth, the site, and the presence or absence of secondary changes and metastases. The more striking features will be mentioned here while the subject will be discussed in detail in the section on general symptomatology of intrathoracic tumours.

The onset is usually insidious and the patient may show symptoms referable to his respiratory system or may only present indications of metastatic growths elsewhere in the body. The most common complaint is cough, at first non-productive, later with expectoration of sputum. Attacks of coughing may be intermittent and dyspnoea may be paroxysmal. Sometimes haemoptysis is the initial symptom and may be persistent and even fatal. In more than half the cases the sputum is blood stained at some period of the disease. Pain occurs in about half the cases, either as a dull aching sensation or in lancinating spasms.

Many patients present themselves with a vague history of slight dyspnoea, cough, and weakness, and are found to have a well marked pleural effusion. In about one third of these examples the effusion is haemorrhagic/

haemorrhagic. The development of a blood stained effusion in a middle aged patient is almost pathognomonic of malignant disease. The majority of cases develop pleural effusion as a later feature. Marked loss of weight and anaemia are comparatively uncommon and are often absent even in the later stages.

Bronchial stenosis is associated with cough at an early stage, at first dry and irritating, but later persistent and with foul smelling sputum indicative of bronchiectasis and abscess formation. With these symptoms there may be fever, and some degree of clubbing of the fingers is often present. The diagnosis of chronic bronchitis in a person of middle age should carry with it the possibility of lung cancer, a lesion which has hitherto received scant attention in such cases.

The most striking clinical feature is sometimes referable to the effects of secondary growths. Instances of symptoms due to metastases alone include come from a secondary nodule in the brain, glycosuria from deposit in the pancreas, acute intestinal obstruction and transverse myelitis. This aspect will receive fuller discussion later.

The duration of symptoms varies according to the character of the tumour. The average duration would appear to be about 6 months, though haemoptysis has been rapidly fatal, coma the first and only indication/

indication of disease, while the history may show evidence of symptoms for several years.

Each individual feature will be dealt with in detail and it has been the intention to give at this stage only a general impression of the symptomatology in correlation with the pathological aspects.

TUMOURS OF THE MEDIASTINUM.

The changes of pathological opinion have been indicated in connection with carcinoma of the lung as to the source of many tumours showing their maximum growth in the mediastinum. The number of neoplasms which are said to originate in this region has thus become more limited as our knowledge has become concise and definite. Formerly the diagnosis of mediastinal tumour, or mediastinal sarcoma where malignancy was evident, was considered sufficient in itself. Modern demands require a more accurate localisation and interpretation of the nature in view of the means of radical treatment to which we now have access. While the malignant growths may still be regarded as fatal in nearly all cases, the benign tumours, which by their mere presence may be harmless, may be sufficient to cause death by their continued growth or by their effects on other structures. The study of the nature of and the diagnosis of the benign neoplasms is of special value in respect of the treatment which may be effectively employed. Growths situated in the mediastinum which have originated in the thoracic wall will be given only brief mention. Special interest is attached to tumours arising from the tissues proper to the mediastina, areolar tissue, lymph glands, thymus gland, nerves and sympathetic trunk and to the group of dermoid cysts and teratomata.

BENIGN TUMOURS OF THE MEDIASTINUM.

Benign growths are rare in this region and are almost as uncommon as in the lung. Available records, however, suggest that they may exist more frequently than is apparent since many examples have produced no symptoms and have only been discovered at autopsy. Mention may be made of the classical publication by Hare in 1889. The collection by this author of 520 cases of mediastinal tumour included 7 fibromata, 3 lipomata, 3 enchondromata and 11 dermoid cysts. In 1926 Heuer, Andrus, and Taylor recorded 135 teratomata (including dermoid cysts), 2 fibroleiomyomata, 2 xanthomata, 18 fibromata, a few examples of lipoma, 9 ganglioneuromata, 13 "hour glass" tumours, and some cases of chondroma. A few additions may be made to these figures but the numbers give some indication of the incidence of benign mediastinal tumour. As in the lung it will be the practice here to mention in detail most of the rarer forms which have been recorded though a complete collection is not intended.

FIBROLEIOMYOMA.

Two cases of fibroleiomyoma have been recorded by Jacobaeus and Einar Key. Both tumours occurred in young men, were situated in the posterior mediastinum and were successfully removed at operation.

So/

So far as can be ascertained there are no other cases of this nature mentioned in the literature.

XANTHOMA.

Xanthoma has been known to occur in the mediastinum in two instances. Wessen has reported one case. Heuer's case may be described fully. The growth, somewhat larger than a golf ball, was removed from the right side of the posterior mediastinum where it had attachment to the tenth rib. There had been a history of cramp-like pains in the right lower quadrant of the abdomen for fourteen years. Removal was easily accomplished, and symptoms disappeared. Microscopical examination showed the typical appearance of a xanthoma composed of connective tissue and "foam cells".

FIBROMA.

Heuer and others have collected from the literature 18 cases of fibroma. Some of these are said to have shown invasive qualities. They are usually found in the anterior mediastinum but three occurred posteriorly. In one example tumours were in both situations (Garré). The fibromata have been attached to the sternum, the pericardium, the ribs or the vertebrae, and in one case to the aorta. They are usually encapsuled/

encapsuled and of firm consistence. Myxomatous degeneration has been seen and cysts sometimes occur.

Dunhill removed a large fibroma weighing 1 lb. 3½ oz., and measuring 13¾ cms. at its greatest diameter. The tumour was situated in the anterior mediastinum and occupied most of the upper part of the right side of the thorax, the lung being displaced downwards. By means of a collar incision combined with vertical section of the manibrium sterni Schwyzer removed an extremely large fibroma from the superior and posterior mediastina of a man aged 43.

Apart from Heuer's series, Harrington has removed two mediastinal fibromata at operation, and Roberts records two cases of fibroma of six benign intrathoracic tumours which he has seen within the last six years.

LIPOMA.

Lipoma of the mediastinum is also rare. Yater and Lyddane reported one case and discovered eleven others recorded in the literature. To this collection several others may be added. Of the above eleven cases, two occupied the superior mediastinum and projected into the neck (Beatson), one was confined to the anterior mediastinum and the remaining growths were situated anteriorly on one or on both sides of/

of the chest. In three examples (Kronlein, Gussenbaum, Beyers) the lipoma was constricted in such a way that one portion presenting externally was connected with the remaining intrathoracic portion by a pedicle which passed through an intercostal space. Garnier and Grosjean found one instance in which the pedicle passed through a congenital defect in the sternum. In most cases the tumour could be readily shelled from its capsule. In others finger-like processes were prolonged to the pericardium and bronchi. Ewing's case was composed of five lobules. The size varied from twice that of a hen's egg to the large lipoma weighing 17 lbs. 6 oz. recorded by Leopold. This series quoted included the cases of Graham and Wiese, Cruveilhier, Bartoli, Fitz, and Lemon, in addition to those already named.

Other cases have been reported and may be mentioned as some resemble those above and others provide interesting features. von Bergmann reported a lipoma consisting of two halves, the intervening portion passing through a congenital defect in the sternum (vide Garnier and Grosjean above). The lipoma noted by Sauerbruch was situated in the anterior mediastinum and attached to the pericardium. The mediastinal growth may, as described by Rokitansky, project into the pleural cavity or extend along the intercostal space. Conner's

case/

case presented a portion of the lipoma on the front of the chest. Czerny has recorded penetration of the posterior thoracic wall, a portion of the growth appearing on the back. Carless found the pedicle of a lipoma of the thyroid region to pass down to multiple fatty tumours in the mediastinum. Finally in the unusual instance of Broca's lipoma, which Wells has recorded, most of the oesophagus was surrounded and compressed.

Of this complete series of nineteen cases, in at least six the lipoma has been successfully removed (Graham and Wiese, Kronlein by von Langenbeck, Beyers, Beatson, Cokkalis by Sauerbruch, Yater and Lyddane). The tumour varied in size and in position, but the majority occurred anteriorly.

Kronlein's example occurred in an infant aged six months, and Beyer removed a lipoma from a boy aged 22 months. Most of the other cases occurred in males of middle age.

Of the series reported by Yater and Lyddane symptoms of pressure on intrathoracic viscera were recorded in only four cases and dysphagia was present in Broca's case. A mass the size of a foetal head, recorded by Fitz, presented no symptoms referable to the growth itself. The patient, a man of 34, died of pericarditis.

CHONDROMA./

CHONDROMA.

It has not been possible to find in the literature any definite record of a chondroma originating in the mediastinum. From the absence of cartilage in the normal subject this is to be expected. Chondromata usually arise from the ribs or spinal column in the region of the costo-vertebral angle or from the sternum or the ribs anteriorly. They may grow slowly into the mediastinum and displace the structures there and may cause deformities such as gibbus, prominent sternum, or localised bulging of other parts of the chest. The tumours are usually circumscribed and encapsuled, are composed of hyaline or fibro-cartilage and not infrequently show myxomatous degeneration. Arising from the thoracic wall these tumours are comparatively rare, are not definitely within the scope of this subject and will be given no further detailed discussion.

GANGLIONEUROMA.

The ganglioneuromata form an interesting type of benign tumour of the mediastinum. Heuer and his collaborators collected reports of nine of these growths and gave as their definition "tumours having, in the majority, a direct connection with the sympathetic system (ganglia or cords)". In all there are

on/

on record sixteen cases of ganglioneuromata situated in the thorax. Some of the examples, like that of Fletcher cited by Dunhill, may have been confused with fibroma involving the sympathetic ganglia or trunks rather than being composed of nerve tissues.

These tumours arise in the posterior mediastinum in the region of the costo-vertebral angle. In the upper part of the chest the growth may occupy the position of one lung apex or may appear equally on both sides. In this series there is no definite predilection for the left side which is found to be the characteristic feature of ganglioneuromata throughout the body. The size has varied from that of a hen's egg to that of a child's head. In the case recorded by Anderson and Shennan the growth was spongy, while Brunner's example was firm with a glistening surface. Several tumours have resembled lipoma in appearance and consistence. Loretz' ganglioneuroma, occurring in a woman aged 35 years, who died after an epileptic fit, presented a hard cartilage-like outer shell containing a soft grey mass. The section of this tumour showed apolar and unipolar ganglion cells, partly isolated and partly arranged in clusters, and non-medullated and a few medullated nerve fibres.

The histological appearance is fairly characteristic. In a loose reticulum of connective tissue there are/

are groups of medullated and non-medullated nerve fibres in varying proportions with scattered unipolar or multipolar ganglion cells. In some cases the fibres may be wholly non-medullated and there may be striking resemblance to a neurofibroma. The ganglionic cells may be very large like giant cells and in shape they may become round and indefinite which causes difficulty in diagnosis. The cells may show degenerative changes and may become distended with myelin. Malignant changes have been noted in a few instances of which the case reported by Delesert will be mentioned under malignant tumours of the mediastinum.

In almost all the recorded cases the patients were young,from twelve weeks to puberty. Persistent or paroxysmal cough and dyspnoea have been the most prominent symptoms. Lilienthal's case had been diagnosed as encysted empyema, but a typical ganglioneuroma, the size of a tennis ball and of greyish colour, was removed from the right side of the posterior mediastinum at operation. The subsequent development of Horner's syndrome indicated injury to the cervical sympathetic nerve fibres. The tumour has been removed in a few other cases.

MIXED TUMOURS.

A few cases are recorded in the literature where benign mediastinal growths have been composed of two/

two or more tissues. Of these the fibrolipoma of Garré is an example. This tumour occurred in the posterior mediastinum and was adherent to the visceral pleura.

Harrington has removed five growths of the nature of neurofibroma. Myxochondromata and osteochondromata have been observed and some examples have been extirpated. These tumours usually arise from the thoracic wall and have already been mentioned.

HOUR-GLASS TUMOURS.

The group of tumours to which this term applies is composed of growths situated along the spinal column, of hour-glass shape with the constriction occurring in the region of the intervertebral foramen. In the collection of papers composing the Cushing Birthday Volume, Heuer, whose contribution has formed the substance of most of this section, has recorded an excellent series of these tumours of which those occurring in the thorax will be discussed here. Although they arise essentially from the spinal membranes, ganglia, and nerve roots, intraspinal epidural fat, ligaments, fasciae, and cartilages of the vertebrae and ribs, and from the sympathetic nervous/

nervous system, these growths form an entity of which the study is justified especially with regard to their diagnosis and treatment.

Heuer has collected 29 examples of hour-glass tumour of the thorax. The pathology is somewhat indefinite, open to doubt in some instances, and has not been recorded in two cases. In this series there are:- large cell sarcoma 2, fibrosarcoma 2, small cell sarcoma 1, angiosarcoma 1, neurofibroma 5, neurinoma 3, neuroma 4, ganglioneuroma 3, extra-dural psammoma 1, fibroma 1, chondroma 3, and osteo-chondroma 1. Even though the histological diagnosis is doubtful in some of these cases, the majority of this group are benign tumours. The size of the media-stinal portion varied from that of a plum to that of an infant's head. Most of the growths were circum-scribed and could be separated from the pleura. In one case only, "pleural neurofibroma", there was local extension to the vena cava and metastases in the spleen. The theories concerning the shape depend for their elaboration on the site of origin of these tumours. They are said to arise without and grow through the intervertebral foramen, to arise intraspinally growing outwards, or to originate at the foramen and develop in both directions. A further theory suggests the presence of the tumour at an early age, subsequent growth/

growth and development of the intervertebral foramen compressing the tumour with the gradual production of the hour glass appearance.

The clinical features of these growths will be dealt with at this stage in order to avoid confusion with the other types of mediastinal tumour in which the features are less characteristic. In 21 cases, where the age and sex are recorded, there were 15 males and 6 females. In the first decade there were two ganglioneuromata and one large cell sarcoma in which the appearance was suggestive of ganglioneuroma. Three tumours occurred in each of the second, third, and sixth decades. The fourth decade showed seven, and the fifth two growths. The youngest patient was $2\frac{1}{2}$ years old and the oldest was 57 years.

Of 21 patients of whom records of the symptoms were available, in nine no symptoms were referable to the mediastinum; eleven had pain, five in the back, and five in the abdomen and side. Cough and dyspnoea were noted in two cases. In almost all cases there was evidence of compression of the spinal cord. Radiographic demonstration was obtained of 16 of the tumours and no records were available in 12. Diagnosis was effected chiefly on radiographic evidence in conjunction with the clinical features of spinal compression.

Most of these cases were submitted to operation and in more than half the tumour was removed at

one/

one stage. In one instance the spinal portion was dealt with at a preliminary stage and the mediastinal portion was removed subsequently; and in a few cases where the spinal portion had not been recognised at first, the mediastinal tumour was extirpated in the first instance. Where the growth received radical treatment the results were good and disappearance of symptoms frequently occurred. Heuer suggested that in these cases laminectomy should be a primary undertaking in order that the extent of the intraspinal portion may be decided, the remainder of the growth being dealt with subsequently or at a later operation.

LYMPHOMA.

Simple new growth arising in the mediastinal lymph glands must be an extreme rarity. Such a tumour is described in the text books as occurring in other situations, but it has not been possible to find any record of a tumour of this nature occurring in the mediastinum.

TUMOURS OF THE THYMUS.

While simple tumours of the thymus gland are rarely mentioned in the literature, the commonest form of benign enlargement is generally the result of hyperplasia, and is frequently of such an extent as to/

to form a definite variety of mediastinal tumour. Although this is not of a neoplastic nature its importance warrants detailed discussion. The few instances of simple tumour of the thymus will also be mentioned.

The thymus arises from the third and fourth bronchial clefts in association with the parathyroid glands. The fully formed organ has the shape of a double pear and is composed of a series of lobules each having a cortex and a medulla, the whole being surrounded by a capsule. The parenchyma cells resemble small lymphocytes in many respects, but Ewing and others have noted definite differences between the two types. The doubt regarding their origin from epithelium has been supported by the existence of evident transition forms between these small round cells and the reticulum cells. This still remains a subject of controversy. The reticulum is derived from epithelium which becomes stretched to form fine fibrils and which is accumulated in places with the production of concentric groups of flattened cells known as Hassal's corpuscles. The supporting stroma is composed of fine connective tissue and blood vessels. Normally the thymus increases in size for the first few years of life, remains stationary until about the twelfth year, and then atrophies so that only a trace remains at the twentieth year.

Thymic/

Thymic hyperplasia has been found to be associated with the condition of status lymphaticus, Graves' disease, myasthenia gravis, idiopathic epilepsy and with some forms of lymphatic leukaemia. Abnormally large thymus may occur unassociated with other abnormality. Moro describes three clinical divisions of enlarged thymus: congenital hyperplasia of the thymus, status thymo lymphaticus and status lymphaticus. The first occurs more commonly in America. Symmers has analysed 249 cases of status lymphaticus from a total of 457 cases observed in 5, 652 autopsies at the Bellevue Hospital, New York. In the first group of 118 cases there was obvious and marked enlargement of the thymus gland, hyperplasia of the lymph nodes, spleen, intestine and elsewhere, hypoplasia of the cardiocascular system, and other irregularities. Histological examination showed hyperplasia of the cortical lymphoid follicles, and, in some cases, engorgement of the sinuses with lymphocytes. The second group,designated recessive status lymphaticus,contained 89 examples in which the thymus was almost invisible to the naked eye and the remaining lymphoid tissue was atrophic. Microscopical examination showed areas of necrosis and fibrosis of the follicles of the lymph nodes, which Symmers attempts to correlate with the state of systemic hypersensitisation associated with sudden death and with epilepsy. A third group, in which a mixture

of/

of the hyperplastic and recessive types was present, was constituted by 42 cases. In the first group, the hyperplastic thymus had caused no sign of tracheal compression in any instance. This is contrary to general belief. Ewing and others claim that, at least in part, the enlargement exerts a mechanical effect in fatal thymic asthma. Janeway noted respiratory stridor in all his cases of thymic enlargement, and Herrick found this a marked feature in the six examples which he described. Perkins found that compression of the trachea occurred also between the gland, the innominate and left common carotid arteries, and the arch of the aorta. In certain positions the thymus is drawn upwards by Piersol's ligament which connects it to the thyroid. As a summary of this question a recent report by the Status Lymphaticus Committee states that an abnormally large thymus in itself cannot be considered an indication of status thymo lymphaticus, that in the relatively few data available there was no evidence of concomitant general hyperplasia of lymphoid structures in cases of abnormally large thymus, and concludes that the factselicited afforded no evidence that status thymo-lymphaticus has any existence as a pathological entity.

Scott Williamson and Pearce, in their conception of/

of the structure and physiology of the thyro-thymic system, have traced an association between the two glands on which are based their theories concerning the toxicity of some forms of goitre. Capelle is quoted by Symmonds as having collected from the literature sixty cases of Graves' disease in which he found thymic hyperplasia in all the instances where death occurred from intercurrent affection, in all cases of death resulting directly from hyperthyroidism, and in all cases of death after thyroidectomy performed to relieve the condition. von Haberer reported eleven cases in which the thymus was removed during operation for goitre. In five the indication for thymectomy was difficulty in breathing which could not be explained by the goitre alone. In four instances operation was carried out for severe goitre and in a fifth thymectomy was performed after no improvement has resulted from thyroidectomy. In every case both local and toxic symptoms disappeared and in each example the thymus showed simple hyperplasia. Kocher and others have written on this striking association while other observers have found no evidence of its existence. The solution to this problem would seem to lie partly in the fact that changes in the thymus gland occur readily after any operation and may result from metabolic disturbances especially in those associated with the/

the thyroid gland.

Bell found thymic enlargement in 17 and thymic tumour in 11 of 57 cases dying of myasthenia gravis. This author's case was found to have an encapsuled tumour composed of cells with large vesicular nuclei and abundant cytoplasm forming a syncitium in the spaces of which there were numerous lymphocytes. No Hassal's corpuscles were seen and the tumour was designated a benign thymoma. Five others of this series were of a similar nature, and of the remainder one tumour was definitely malignant (Meggendorfer). In the latter case myasthenia gravis was associated with enlargement of both thyroid lobes and with a malignant thymoma. In the cases reported by Schumacher and Roth, myasthenia, exophthalmic goitre, and thymic enlargement occurred simultaneously.

Apart from the cases collected by Bell the literature contains few references to benign thymic neoplasms, which are rare. Winogradoff and Caso have each described congenital myxomata of the thymus in children. In the latter case the tumour had reached a large size, and in both the microscopical examination showed large numbers of lymphocytes and Hassal's corpuscles.

Cysts of the thymus are rare. Bednar described a case in which each lobe was converted into a large cyst (Ewing). Hueter found multiple cysts lined by flattened/

flattened cells with polypoid masses of thymic tissue, mucoid and lipoid material in the lumina. A mediastinal cyst lined by ciliated epithelium and having thymic tissue in its wall was described by Westernak (Heuer et al.). Soupault found the lower half of a hyperplastic gland, in a case of Graves' disease, to be composed of small cysts filled with mucus. Dermoid cysts have been noted by Hare, and Rolleston found a cystic tumour with areas of cartilage, structures resembling Lieberkukn's follicles and sarcomatous elements. Siedel describes an enlarged thymus of a child, aged 2½ years, as consisting of multiple small cysts lined by fat endothelium and containing sanguineous fluid. A dermoid cyst removed by Wolfsohn from the thymus of a female aged 34, had caused rarefaction of the sternum.

Whilst the entity of the status thymico-lymphaticus would appear to be doubtful it may be concluded that abnormally large thymus, constituting one variety of mediastinal tumour, may occur either as a form of hyperplasia, of persistence of its early state, or in association with some other conditions, may be rarely due to benign new growths, and in any of these forms may give rise to symptoms requiring definite treatment.

INTRATHORACIC GOITRE.

The thyroid gland occasionally assumes, wholly or in part, a position in the mediastinum. When this intrathoracic thyroid tissue becomes the site of pathological changes or more rarely of physiological enlargements, symptoms may arise both locally and generally. It is not thought necessary to enter into details of the various forms of enlargement which may occur nor is there need to consider at length the general effects which the pathology of the gland may determine. Briefly, the enlargement of the thoracic portion of the thyroid may be unaccompanied by similar changes in the cervical portion and may encircle or compress the trachea without any change in appearance of the neck and so assume the characters of other forms of tumour of the superior mediastinum. Where the intrathoracic thyroid constitutes the whole gland tissue the considerations with regard to treatment will be modified. The retrosternal goitre is usually found as an ovoid tumour situated entirely behind the manubrium or presenting in the episternal region. The consistence varies according to the pathological changes, may be firm or soft, solid or cystic, and the surface may be smooth or nodular. Haemorrhage into a cyst may produce sudden increase in size with corresponding increase in the symptoms. Calcification in/

in the gland may be evident and malignant changes occur rarely. Though uncommon this condition must be considered as a possibility in the diagnosis of tumours in the anterior mediastinum. Where accurate diagnosis is not possible it may be necessary to explore the normal situation of the thyroid gland before proceeding with the operation for removal of such a tumour. Prior to removing an intrathoracic fibroma Dunhill found this a necessary step.

MEDIASTINAL CYSTS AND TERATOMATA.

Several cases have been reported where simple cysts have been found in the mediastinum. These have usually been composed of epithelium ciliated or non-ciliated, lining a cyst cavity containing mucoid material. The cysts have been surrounded by an adventitious capsule. Other cases have shown a more complex structure and greater differentiation of tissue, the lining membrane closely resembling in section that of the gastro-intestinal tract. Still further there is the group of dermoid and teratomatous cysts which form the commonest and perhaps the most interesting of the benign mediastinal tumours. The simpler cysts will be dealt with in the first place and the dermoid cysts and teratomata will then be discussed.

Christian noted in the literature twelve instances

of/

of ciliated epithelial cyst in the mediastinum. Of these six were situated in close proximity to the bifurcation of the trachea, four were found at the lower end of the oesophagus, and one occurred in the anterior mediastinum above the tracheal bifurcation. Most of these cysts were small and produced no symptoms. Bramwell's case, a middle aged man, presented a visible pulsation over the second right interspace and the mediastinal cyst was discovered at autopsy. Heuer quotes Fletcher who reported the death of a child, aged six years, after cough had been present for only a week. Sauerbruch has recorded two cases of which the details are illustrative. In the first, a large cyst containing greyish yellow colloid material was situated in the anterior mediastinum of a female, aged 30, who had complained of dyspnoea and cough, and who showed cyanosis of the face. The cyst was adherent to the superior vena cava and the wall showed a haemangiomatous appearance in some areas. In the second case where a man, aged 43, had complained of shortness of breath and pain for six months, a cystic tumour was found in the anterior mediastinum displacing the heart to the left. After several operations the cyst wall was removed and the patient recovered. Tudor Edwards removed a cyst which was adherent to the pericardium, the lung and the diaphragm. The

wall/

wall had no cellular lining and the cyst was thought to have been a pericardial diverticulum.

Mixter and Clifford have recorded three cases of mediastinal cyst of a rather more complicated structure. The first concerned a male infant, aged 22 months, who had had "pneumonia" on the right side. At operation a cyst was found to extend from the diaphragm to the region of the right apex and was removed in two stages. Section showed the wall to consist of typical gastric mucosa, plain muscle layers, and nerve trunks. The second patient was a male child, aged 7 weeks, who had persistent difficulty and distress during feeding. Death occurred at the age of 14 months. At autopsy an isolated cyst situated at the right apex was found to be composed of deep branching glands, smooth muscle, and a serous coat. The structure was similar to that of the gastrointestinal tract. The third case which these authors record is that of a female child, aged 3 months, who died after several attacks of wheezing and cyanosis. A cyst situated below the bifurcation of the trachea was composed of a fibrous tissue covering, epithelium pseudo-stratified, columnar, ciliated, and in places cuboidal, with a small mass of cartilage and smooth muscle in one area. These cysts were accordingly deemed to be of gastrogenic origin in the first two cases and of bronchogenic origin in the third/

third case. Swanson, Platon, and Sadler have recorded the occurrence of a cyst resembling the first of Mixter and Clifford in which the lining appeared to be of gastric mucosa covered by cartilage. In this instance the origin may be cited as both gastrogenic and bronchogenic.

These cysts have been found in patients of all ages, the last four having occurred in children and the remainder in adults. In contrast to dermoid cysts, the radiographic shadow is only slightly opaque, and the contents are milky, viscid, and mucoid, but are never sebaceous. The latter feature serves to preserve their entity as cysts of mainly entodermal rather than of epidermal origin. Their presence is generally attributed to the pinching off of a bud or diverticulum of the foregut, the trachea, or the oesophagus, which is carried down by the lung. In view of their more regular and decided structure it is less probable that they may arise as a one-sided development of a teratoma.

The origin of dermoid cysts, and of cystic and solid teratomata of the mediastinum has been a subject of much controversy. It embraces the larger question of the source of teratomata in general. These tumours are conventionally studied as one group often without any attempt at dissociation into their component types, which, as Heuer remarks, may be quite distinct from the standpoints of pathology, symptomatology, and treatment.

The/

The gastrogenic or bronchogenic sources of some of the simpler cysts have been traced, and examples where these sources have been combined have been described. Some dermoid cysts consist only of tissues originating from ectoderm. Others are of a similar nature but contain also bone, cartilage, and other tissues derived from mesoderm. The latter are the more common. Finally the teratomata, which may be cystic or solid, are typically of tridermal origin and the tissues may be numerous and complex.

The origin of dermoid cysts has been variously ascribed to preponderance of the corresponding tissues of a teratoma which results from the displacement of a cell or of a group of cells of totipotent characters, to the development of cells isolated during the closure of the pre-cervical sinus, and to the inclusion of ectoderm during the union of the two halves of the body to form the coelomic cavities. It is possible to associate examples of these tumours with each of these theories. That some of these cysts may be associated with the embryonic pre-cervical sinus is quite possible on consideration of the analogy of the branchial cysts of the neck, which possess a similar structure. The third theory of the origin is illustrated by the case, described by von Bergmann, in which a dermoid cyst had been separated into two

portions/

portions one in front of and the other behind the sternum, which was cleft owing to failure of union of the two halves. Carrick, Robertson and Bevan Brown have also removed a dermoid cyst from the anterior mediastinum of a patient who presented a bifid sternum. Bland Sutton has suggested that dermoids may arise from faulty coalescence of the sternum. Some observers have stated their belief that all mediastinal dermoids are in reality tridermal teratomata (Ekehorn). Though usually situated in, and probably originating in the mediastinum, some of these cysts are found at the base or between the fissures of the lung, and it is supposed that this selection of site has been due to the attachment to some particular structure whose growth has carried the cyst from the middle line.

Dermoid cysts and teratomata, though comparatively rare, are the commonest types of benign tumours of the mediastinum and of all benign intrathoracic growths. Malignant changes may be superimposed and will be referred to later. In 1929 Heuer, Andrus, and Taylor were able to collect 138 cases of dermoid cyst and teratoma which had been recorded in the literature up to that date. Of 108 cases collected by Smith and Stone, 41 occurred in females, 43 were found in males, and/

and the sex was not noted in 24 cases. These observers described in detail two teratomata, one occurring in a child, aged $4\frac{1}{2}$, and the second in an infant aged one year and eight months. The latter tumour showed signs of malignant changes. They also noted eight other examples which occurred in children. In 82 cases in which the age was recorded the incidence in decades was 6, 16, 43, 7, and 7 over 40 years. From these figures it will be seen that the majority (over 50%) became evident during the third decade of life. This series is partly overlapped by that of Hertzler who collected 73 cases in which the age incidence was similar and the sexes were equally affected. Aurousseau found that 33 of 85 cases occurred between the ages of 17 and 30 years. Caldbick states that there is no sex preponderance and the symptoms usually became evident between the 15th and 30th years.

The size has been found to vary from that of a marble to the large teratoma 15 x 11 x 9 centimetres described by Smith and Stone. In 69 cases where localisation was accurately stated, Aurousseau adopts the classification of Duval and records the positions as 14 retrosternal, 14 cervico-retrosternal, 6 mediastino-thoracic, and 35 lateral thoracic. The lateral thoracic group were described as lying largely in one half of the thorax.

The/

The teratomata may be cystic or solid, and the dermoid cysts may be unilocular or multilocular. The so-called epidermoid type is characteristically composed of an adventitious connective tissue covering lined with epidermis, containing hair follicles and sebaceous glands. Cellular debris, sebaceous material, and hair are present in the interior. The lining epithelium may be smooth or may show polypoidal projections. Most of the typical dermoid cysts have, in addition to ectoderm, various forms of connective tissue, bone, cartilage, muscle, and teeth in the various stages of development. The latter is the type most commonly found and the combination of both ectodermal and mesodermal tissues would indicate an origin other than simple ectodermal inclusion. The epidermoid and dermoid types are to some extent distinct from the more complex teratoid tumours and cysts though it has been stated that more careful examination of all these growths would reveal the presence of ectodermal, mesodermal, and entodermal elements.

The complex teratomata may contain almost any variety of tissue which is found elsewhere in the body. Nervous tissue, ganglion cells, nerve fibres, tissue resembling the choroid tissue of the eye, intestinal epithelium, ciliated epithelium sometimes lining cysts, lung/

lung alveoli; connective tissue of all kinds, foci of bone, cartilage, may all occur in irregular formation and in various degrees of development. Portions of thyroid are not uncommon.

The secondary changes with which these tumours may be associated form an interesting aspect of their behaviour. Growth may continue to such an extent as to cause bulging of the chest and marked displacement of the intrathoracic viscera. Kyphosis was produced in Le Wald's case. Nandrot found that breathing was almost impossible in a patient who had a multilocular cyst weighing 22 lbs. Rupture of a cyst may occur into a bronchus with evacuation of some of the contents. In eight cases mentioned by Hertzler hairs and fatty material were found in the sputum. The cyst may also rupture into the pleural cavity and empyema has resulted. In one of the examples described by Smith and Stone hairs were found in the fluid aspirated from a pleural effusion. The latter is not infrequent and adhesions surrounding the growth are an almost constant finding. Close attachment to the pericardium, diaphragm, and to the great vessels has lead to difficulty at operation, though pleural adhesions have constituted an advantage. The surrounding reaction may be due to irritation from the contents of the cysts or to infection. Abscesses have been found in the tumour itself and have lead to infection of the lung or pleura.

Ulceration/

Ulceration has produced sudden haemorrhage which terminated fatally in five of Roger Morris' series, while one of Heuer's examples had empyema and presented a discharging sinus in the root of the neck. Lilienthal has indicated the effect of a comparatively small dermoid cyst of the mediastinum which obstructed a main bronchus and produced bronchiectasis. It was not until lobectomy had been performed for this condition that the cyst was discovered to be the causal factor. Calcification of the cyst wall has been noted and Heuer maintains that the calcified shell which he removed from the right basal region of a patient, aged 53, was the existing remains of a dermoid cyst. Though no cellular elements could be found in the wall the cavity contained cholesterol crystals and fatty detritus. It is possible that this shell may have been the final stage of an encysted pleurisy or empyema, an example of which the writer has recently seen.

Hertzler found malignant changes in four examples of his series of 72 cases, and Roger Morris noted similar processes in five of 57 cases. Heuer mentions that sarcoma is found more commonly than carcinoma in those tumours showing evidence of malignancy. Beal recorded carcinomatous changes in a dermoid cyst, while the teratoma of Smith and Stone showed surrounding infiltration by carcinoma cells having an alveolar structure/

structure. Maxwell found evidence of carcinoma in one dermoid cyst while a second presented sarcomatous elements.

MALIGNANT TUMOURS OF THE MEDIASTINUM.

Primary malignant growths of the mediastinum are comparatively rare. Ross states that 80 out of 20,745 patients admitted to the Brompton Chest Hospital during the period 1900-1913 were suffering from malignant disease in the mediastinum. In sixty of these cases autopsy was performed and histological examination was made. Forty-four cases were found to be sarcoma, of which 32 were said to be lymphosarcoma and only ten instances of carcinoma were recorded. Most (68%) of the cases involved the anterior mediastinum, neither lung was affected in four, while 93.3% of cases showed involvement of one or both lungs. Men were affected more frequently than women in the ratio 2.15 : 1. In the females carcinoma occurred three times as often as in males. In Ross' paper, which is much quoted, there is no description of the histological details and the brief notes of the gross features may be readily applied to growths originating in the bronchi as well as to those arising primarily in the mediastinum. In the light of recent knowledge of cytology of lung cancer/

cancer an entirely different view would probably now be held as to the nature and origin of many cases of the series quoted. In any case, the figures of incidence, 80 out of 20,745, .004% of cases treated at a chest hospital, would indicate that malignant mediastinal tumours are rare.

Excluding the oesophagus, the heart, and the pericardium, the sources of mediastinal cancer are limited to the thymus, lymph glands, nervous tissues,connective tissue, and to benign tumours. Those arising from the last three sources are so few as to warrant individual mention. It is to the thymus gland and to the lymph nodes that the origin of most primary mediastinal cancer is attributed. Much has been written on this subject and the difficulties of differentiation between tumours derived from these two sources still exist. The interpretations of the histological features and the staining reactions show wide variation on the part of different observers. In the thymus the cells which may give rise to malignant growth are the small round cells, often spoken of as lymphocytes, the reticulum cells which are of entodermal origin, and the connective tissue of the stroma. The origin of the small round cells of the thymus is debatable and their distinction from true lymphocytes is not unanimously admitted. Shennan has emphasised the fallacies of staining reactions and of dogmatic diagnosis relying/

relying solely on some specific feature such as intercellular reticulum or nuclear staining. Ewing has studied thymic tumours at considerable length, and points out the differences between the small round thymic cells and the round cells found in tumours of lymph nodes. While the latter are true lymphocytes, he ascribes the former to an origin from reticulum cells which form the chief or sole source of the round cells constituting the lymphosarcoma or thymoma. Though the true lymphocytes may be in abundance or may be few in number, Ewing maintains that they play a comparatively passive part.

The phenomenon of pleomorphism has lead to errors in interpretation of the nature of thymic tumours. Carcinoma is said to arise from reticulum cells but it is difficult to differentiate some of these examples from the lymphosarcoma or thymoma indicated above. Sarcoma may rarely arise from the connective tissue stroma. The existence of cells in stages evidencing transition from the reticulum cell to the lymphocyte has lead to the belief that the latter may arise from reticular epithelium. Against this theory many observers have shown differences in behaviour and staining reaction between the true lymphocyte and the small round cells both of which co-exist in the thymus. True lymphocytoma has been little mentioned in view of these findings.

Tumours/

Tumours of the lymph glands may arise from the reticulum cells or from the lymphocytes. The prevailing uncertainty as to the morphological relationship between these two cells and the pleomorphism which the former type so often shows render it difficult to dissociate the two types with any degree of accuracy and, as such distinction would be unnecessarily complicating in the light of indefinite knowledge, the lymphosarcoma arising from reticular epithelium and the lymphocytoma from the lymphocyte may well be considered together.

Finally the situation with regard to the pathology of these tumours becomes more complex by the association with the so-called malignant form of Hodgkin's disease, which is found to affect both the thymus and the lymph glands. Indeed Ewing has concluded that the "great majority of thymus tumours, and especially the mixed growths, represent infectious granulomata or particular forms of cell overgrowths arising on the basis of granuloma". The same observer is also of the opinion that most of the mediastinal lymphosarcoma arise from the thymus and are to be considered as varieties of thymoma.

THYMIC TUMOURS.

It is difficult to formulate an accurate impression of the incidence of tumours of the thymus. Careful analysis of the literature by Foot in 1926 showed/

showed that 81 cases of malignant thymic tumour had been reported. Heuer, in whose personal experience of 30 cases of intrathoracic tumour there was only one mediastinal lymphosarcoma, amplifies these findings by the statement that the existing number of reports is under a hundred. Out of 60 cases of intrathoracic cancer recorded by Schuster, 5 were diagnosed as thymomata,

Maxwell found no example of thymoma but there were 8 cases of mediastinal sarcoma in 239 intrathoracic tumours. The close association with primary tumours of the lymph glands may modify these figures, but it will be seen that both are relatively rare types of malignant disease.

The age incidence is variable. Eighteen of the 33 authentic cases recorded by Rubaschow were under twenty-five years of age. Ewing's three examples were 19, 32, and 50, while Foot's patients were 2, 9, and 38 years. Shennan's five cases occurred in patients aged 27, 30, 36, and two young adults, of whom four were males and one was a female. Delesert records malignant tumours of the anterior mediastinum in three males and three females, aged $5\frac{1}{2}$, 12, 16, 27, 27, and 38 years. Helvestine saw thymomata in a female of 18 and in a male aged 25. Most of the cases therefore occur in patients under thirty years of age.

An/

An objection has been raised by several authors that the diagnosis of thymic tumours has been based on the site of the growth, a question to which reference has been given with regard to mediastinal extension of lung cancer. Ewing asserts that there is little difficulty at autopsy in distinguishing thymic growths from other tumours involving the mediastinum. They are situated in the anterior mediastinum and may reach from the root of the neck to the diaphragm. The trachea and bronchi may be encircled and compressed and the great vessels may be obstructed. The growth may maintain the normal pear shape of the thymus to some extent or may be globular. The surface may be smooth or nodular, and the tumour often exhibits a characteristic pale yellow colour, which may be modified by areas of haemorrhage or by brownish foci of softening. The consistence is usually firm, and on section dense fibrous septa may be seen to produce lobulation. The more rapidly growing tumours are softer, but others may show a marked degree of fibrosis. The vascularity varies but is not usually great. Many of the more malignant growths erode the sternum, trachea, and blood vessels, extend to the pericardium and lungs, while spread to the supraclavicular and axillary glands may be an early feature. The less malignant types tend to remain encapsuled and in these cases enlargement preserves the normal shape of the gland.

In/

In one of Shennan's cases the walls of both ventricles were invaded. Another case showed a large tumour filling the thoracic inlet and metastases in the pectoral, axillary,and para-aortic glands, and nodules in the spleen. In a third of the five examples described by this author there was thrombosis of the left pulmonary artery and vein. In most of the five cases which he recorded, Delesert noted that the vessels were infiltrated and that the lungs,though displaced,often escaped involvement. One of these cases was called lymphosarcoma of the thymus, one large-cell sarcoma, and the remainder were designated lymphosarcomata. The position of the growth together with the nature of the cells, in spite of the absence of thymic elements such as Hassal's corpuscles, indicated a thymic origin. Each of the five cases showed penetration of the veins; internal jugular, superior vena cava, pulmonary and azygos veins, being the most commonly affected. The arteries are less frequently involved. Duguid and Kennedy described a white lobulated tumour extending from the lower margin of the thyroid to the pericardium, enveloping the superior vena cava and carotid arteries,and surrounding the trachea opposite the seventh cervical vertebra. The deep cervical and tracheo-bronchial glands were enlarged. This description is typical of the appearance/

appearance presented by that type of thymoma. Ewing found invasion of the breast in one instance and pleural effusion occurred in another case. The latter has also been noted by Delesert, and empyema was found in one of Shennan's cases. Collapse of the lung has been observed by Delesert and others, and evidence of compression of the vagus and phrenic nerves has been seen. Infiltration of nerves does not usually occur.

Metastases are not usually of wide distribution. A minority of cases have shown wide secondary deposits but the spread is more often confined to the mediastinal lymph glands, the cervical, and axillary groups. Occasionally metastases have been observed in the pleura, liver, kidney, spleen, adrenals, ovaries, pancreas, and brain. Duguid and Kennedy observed nodules in the pleura, epicardium, ovaries and pancreas, and Shennan found secondary growths in the spleen and para-aortic glands. Metastasis in the humerus with pathological fracture is recorded by Zniniewicz, and involvement of the brain by Meigs and de Schweinitz. It is noteworthy that even in cases where growth has been advanced and widely infiltrating there have been no distant metastases. The type designated carcinoma is said to be more prone to distant spread, which however is less marked than in carcinomata of other organs.

HISTOLOGICAL/

HISTOLOGICAL FEATURES.

The histological features show great variation. The association with a malignant form of Hodgkin's disease is evident in the minds of many writers. In his collection of cases of intrathoracic cancer Duguid has omitted all growths "with the large lymphadenoma cell". Delesert has laid stress on the presence of the cells with large nuclei, known as Sternberg's cells, and oesinophil cells as indicative of the thymic origin of a tumour.

The classification on histological grounds presents much difficulty. The structure may show considerable variation. The thymoma of small-cell type is largely composed of round or polyhedral cells having some resemblance to small lymphocytes but differing from the latter in having a vesicular nucleus, well developed nucleoli, and acidophil cytoplasm. Lymphocytes may be present in large masses or may be comparatively few in number. The round thymic cells are said to originate from the reticular epithelium; they show marked pleomorphic characters. According to the beliefs of some authorities their similarity to lymphocytes may be evidence of a definite morphological relationship. They may assume cubical or columnar shapes and attempts at the formation of Hassal's corpuscles may be seen. The reticular cells themselves

may/

may be large and rounded like large sarcoma cells, and peritheliomatous arrangements have been noted. Giant cells are frequently found in thymic growths. They are said to be of two types, some having pale staining, vacuolation, and engulfed red cells, and others of a type resembling the myeloid giant cell, with many vesicular nuclei and opaque acidophil cytoplasm. Both types are usually larger than but may have been confused with the giant cells of Hodgkin's disease. Janeway describes a thymic tumour which contained numerous giant cells and which was designated giant celled thymoma. Some tumours are composed entirely of the small round cells, are of fairly rapid growth, and are usually of the infiltrating variety of thymoma. Erosion of the sternum is not infrequent. As a general rule the course of the disease is short, but the more rapidly growing cellular tumours are the most responsive to irradiation. Other tumours present very few or no small thymic cells and are composed entirely of larger cells of the epithelioid type with a vesicular nucleus which have been mentioned above. Again these may have giant cells and lymphocytes in association. To the appearance which is presented Shennan has given the name "malignant thymoma of the lymphadenoma type", and he found that four of his five cases conformed to this type.

In/

In several of these Hassal's corpuscles were noted. The stroma is variable. Some cases show well marked fibrous strands. In the small celled type the stroma is more often scanty and poorly formed. In the case recorded by Duguid and Kennedy, Bielschowsky silver stain showed a distinct intercellular reticulum.

Carcinoma of the thymus is identical in structure with many of the thymomata of the reticulum cell type and must be ascribed to growth from these cells. On morphological grounds all these growths should really be grouped as carcinomata. The appearance is identical with that described above where the cells have assumed a cuboidal or columnar shape. The cells may occur in sheets and alveolar formation may rarely be found. Concentric arrangements of cells resemble Hassals' corpuscles. Invasion of surrounding organs is said to be less active than in the cases of small round cell thymomata and response to radiation is less definite. Few definite examples can be found. The difficulties of dissociation, if this is possible, of the various forms of lymphosarcoma or thymoma and carcinoma have been described, and confusion may also arise with regard to secondary carcinomatous growths in the thymus. In 1922 Jacobson collected 21 cases of thymic carcinoma from the cases reported in the literature. Whether designated thymoma or carcinoma probably/

probably all these tumours arise from the reticulum cells and are in any event comparatively rare.

Several cases have been recorded where a small round celled thymoma has been associated with lymphatic leukaemia. In Janeway's case the thymus was said to be the site of a lymphocytoma. The patient, a boy aged 8 years, was found to have a marked leucocytosis of 143,000 lymphocytes per cubic millimetre.

Sarcoma of the thymus arising from the connective tissue of the stroma may well have been confused with other types of thymic tumour. Heuer notes 11 cases of sarcoma in Rubaschow's series of 69 cases of tumour of the thymus, but Ewing states that there are strong grounds for concluding that the so-called spindle-cell sarcomata are actually varieties of thymoma. In a study of recent literature it has not been possible to find an authentic case of primary sarcoma of the thymus.

TUMOURS OF THE LYMPH GLANDS.

It is difficult to estimate the incidence of malignant tumours having origin in the mediastinal lymph glands. Many of those growths which were formerly referred to as mediastinal tumour or sarcoma of the mediastinum are now known to have arisen from the lungs. The study of the "oat cell" tumours by

Barnard/

Barnard and others has shown that these growths probably have their origin in the bronchial epithelium. Duguid and Kennedy, however, assert that oat cell forms in a mediastinal tumour must not necessarily indicate a bronchial origin, and describe a case in which these cells occurred though the evidence pointed to origin in lymph glands.

The cells which may give rise to neoplasms are the lymphocytes, the reticulum cells which line the sinuses, and the cells of the connective tissue stroma. It has already been shown in reference to the thymus that the relationship of the lymphocyte and the reticulocyte is imperfectly understood and that the small thymic cell and the lymphocyte may have structural differences which belie close relationship. The same difficulty with regard to the former two cells concerns the lymph glands, while sarcoma arising from the third source must be excessively rare. Ewing states that the majority of the lymphosarcomata are in reality of thymic origin but that the tumours can be dissociated. Graham mentions that tumours arising from the lymphocytes, that is to say true lymphocytomata, are very rare, and that of growths arising from the reticulum cells the most important is the large cell lymphosarcoma. In view of this dubiety it is well to consider these tumours together on a general basis without/

without any definite attempt at classification.

MacCallum has observed three cases of mediastinal lymphosarcoma derived from the lymph glands. In a careful study of the pathological details of 239 cases of intrathoracic cancer, Maxwell found no instance of thymoma, and 8 sarcomata of the mediastinum in each of which the anterior and posterior mediastinal glands were said to have been primarily affected. The individual diagnoses were 3 small round-cell sarcomata, 2 mixed-cell sarcomata, one large round cell sarcoma, and two lymphosarcomata. From these few quotations the impression which has already been conveyed of the rarity of this group of tumours, especially in comparison to the frequency of carcinoma of the lung, will be amplified. Like the thymic growths, the primary malignant lymph gland tumours occur most commonly during the second and third decades and there does not seem to be any predilection for either sex.

These growths tend to form nodular masses and to remain localised to the thorax. They are not confined to the anterior mediastinum in the manner which is more characteristic of the thymomata. The extent of invasion of surrounding tissues shows much variation, and typical features are the envelopment of the trachea and bronchi, and invasion of the pericardium. Less rarely the heart wall is infiltrated. The arteries

do/

do not usually show the complete penetration which is commonly seen in the veins. Spread to the pleura resembles that described under thymomata, and the lung is displaced, or infiltration may occur along the septa and bronchi. The pleura may show miliary nodules and the oesophagus may be eroded. More rarely there are isolated secondary growths in the lungs and occasionally metastases are found in the liver.

The histological features are similar in many respects to those of the thymomata. The type cell is most frequently of the lymphocyte variety and there is little pleomorphism, the cells tending to be alike. Variations towards endotheliod structure are sometimes seen and may indicate origin from the reticular epithelium. The cells are usually small, but may be of medium or rarely of large size. The nuclei are compact or vesicular and are always hyperchromatic. There is a basis of reticular tissue and a variable amount of intercellular stroma, which is sometimes increased to form dense fibrous strands.

Duguid and Kennedy reported an example of lymphosarcoma which was described as an irregular lobulated mass of glands situated in front of the left bronchus, displacing the anterior part of the lung, infiltrating the lung margin and the pericardium, and occluding the vena cava. There were no metastases. The cells were/

were of the oat shaped type with very little intercellular stroma. Ewing refers to four cases, reported by Schlagenhaufer and Kundrat, in which extensive infiltration of the oesophagus had occurred.

SARCOMA OF THE MEDIASTINUM.

Sarcoma arising from the connective tissue of the glands or of the mediastinum is exceedingly rare and is more often associated with malignant change in benign tumours. The cells are usually round or spindle-shaped. In a case described by Shennan the growth had infiltrated the right auricle almost occluding the tricuspid valve, and there were secondary nodules in the lung and liver. The cells were spindle-shaped and were said to have had origin in the connective tissue of the glands. Ewing mentions a liposarcoma which produced metastases in the deltoid muscle and fragments of tumour in the sputum. Tudor Edwards removed a specimen of chondrosarcoma of the mediastinum. The tumour had originated from the second and third ribs and formed an ovoid mass which occupied the upper part of the right side of the chest.

Delesert has recorded a ganglioneuroblastoma in the anterior and posterior mediastina of a child, aged $5\frac{1}{2}$ years. Compression of the trachea, oesophagus, and/

and great vessels was marked and the heart was displaced. Metastases were noted in the tracheo-bronchial glands, supra-clavicular glands, vertebrae, and liver. The tumour was surrounded by a connective tissue capsule and consisted of ganglion cells and nerve fibres.

SYMPTOMATOLOGY.

The benign tumours of the mediastinum may obtain a large size without any indication of their presence. The symptoms to which they give rise are largely dependent on their situation and on the effects which they produce on surrounding structures. General as opposed to local symptoms usually result from the complications which have arisen rather than from the growths themselves. It is intended to give here only a general account of the main features as the detailed study will be made of the symptomatology of intra-thoracic tumours in a later section.

Growths situated in the anterior mediastinum, whatever may be their nature, may so obstruct the thoracic inlet in virtue of their size as to cause compression of the trachea and great vessels. In the case of the malignant tumours this may increase in severity very rapidly and the course of the illness is usually of short duration. Cough may be produced by pressure on the trachea, bronchi, or phrenic nerves.

It tends to be of the brassy hollow type in the first two situations, and is dry at the commencement. Catarrhal changes in the mucosa invariably follow, even in the benign lesions, and there is some expectoration of sputum which may be bloodstained. Coughing may be spasmodic and brought about by exertion. Inspiratory stridor is characteristic of thymic enlargement and formed a prominent symptom in most of the recorded cases. Herrick found marked stridor in six cases of thymic hyperplasia in children aged 1 week, 2 weeks, $2\frac{1}{2}$, 12, and 36 months.

Subsequent infection of the bronchi may lead to bronchiectasis with loss of weight, slight fever, expectoration of foul-smelling sputum. Less commonly lung abscess is produced. Haemoptysis is rarely profuse but has been sudden and fatal in a number of cases including dermoid cysts as well as malignant tumours. The sputum may show evidence of the nature of the growth, hairs and fatty material indicating the presence of a dermoid cyst, and portions of necrotic tumour tissue suggesting a malignant condition.

Pressure on the veins is associated especially with the malignant tumours of the anterior mediastinum. Prominence of the cutaneous veins of the front of the chest and down the side of the trunk is often an early sign. Cyanosis and oedema of the face and of one or both arms may occur at a later stage. Pressure on

nerves is seen more commonly in cases of malignant growths. The cervical sympathetic nerve has been affected but is more frequently involved by aneurysm. Paralysis of the diaphragm has occurred and occasionally the recurrent laryngeal nerves may be irritated or paralysed. More remote results of pressure on the intrathoracic structures include pleural and pericardial effusion, which may arise as a result of obstruction of the azygos or intercostal veins, of spread of malignant cells, or may be due to infection. Empyema has occasionally been seen but the effusion is more commonly serous or sanguineous. Except with regard to the hour-glass tumours nervous symptoms are uncommon. The vertebrae and ribs may rarely be eroded by benign growths. Ulceration at the root of the neck or of the chest wall is not unusual as a late feature in malignant tumours. Pain is found in about a third of the cases but is not a prominent symptom. The retrosternal pain noted by Kaulich and Rendu has not been a common feature of thymic growths.

In the malignant mediastinal neoplasms enlargement of the supraclavicular and axillary lymph glands is often early and the course of the disease may be rapid; oedema and cyanosis of the face and arms, cough and extreme dyspnoea progress to an early death from asphyxia or from pneumonia. Symptoms from metastases are rare, and the general condition is consequently/

consequently remarkably good until the final stages. By contrast, the symptoms resulting from benign tumours may be much prolonged with chronic ill health suggestive of phthisis, marked toxaemia and loss of weight associated with concomitant infection, and most of them eventually prove to be fatal if untreated.

INTRATHORACIC TUMOURS.

CLINICAL FEATURES.

The symptoms and signs of tumours within the chest vary widely in accordance with their nature and situation. The malignant growths may present features less striking and less severe in the moderately early stages than are evidenced by other tumours benign in nature but equally harmful and no less fatal in their issues. The manifestations are modified according to the changes within the growths and to the character of their secondary effects. It is safe to say that, within certain limits, no single type of intrathoracic tumour is characterised by any definite symptom or group of symptoms. The hour-glass tumours form one exception to this statement and on these grounds their detailed symptomatology has already been dealt with. The benign tumours of the lung, the rarer forms of intrathoracic cyst, and simple enlargement of the thymus have also been considered and illustrated by descriptions of individual cases. An attempt will be made to summarise the more common features of the two most important series, the malignant growths of the lung and the mediastinal tumours, and each of the clinical findings will be discussed in greater detail.

Different observers have adopted attitudes and standards/

standards which are not strictly comparable from the standpoint of tabulation. Some authorities have recorded the clinical findings in cases reviewed post-mortem, but it may be assumed that in the majority of instances the case histories were taken on or shortly after admission to hospital. While the accuracy is not strict, the results obtained from Table X are worthy of review as an indication of the frequency with which the various symptoms are met in a large series of cases. For the most part, the numbers indicate those symptoms which have been especially striking either on admission to hospital or when the patient first sought advice. Naturally the advance of the disease would lead to an increase in number and severity of symptoms. The percentages have been calculated from the collection of series where definite note has been given of the specific symptom. With regard to dermoid cysts, teratomata, and malignant tumours of the mediastinum the figures are less complete but are representative and are given for purposes of comparison.

MODE OF ONSET.

The clinical features of cancer of the lung vary according to the localisation and rapidity of growth, the degree of ulceration and obstruction, the association/

association of infection, and to the presence and site of metastases. In most instances the onset is insidious. More rarely the disease is manifested suddenly by haemorrhage, or by such nervous symptoms as hemiplegia coma and convulsions. For practical purposes the cases may be grouped into those in which the onset is insidious with symptoms referable to the respiratory system, or with features more especially of disturbance of other systems; and the cases which begin their course suddenly with obvious affections of the chest, or with no striking evidence of intrathoracic disease. These four groups will be studied briefly.

(1) Cases with insidious development of respiratory symptoms. It is to this group that most of the cases belong, and in which many difficulties are met with regard to diagnosis. In a large number there is a history of a recent attack of influenza or pneumonia with subsequent ill health, although there may have been a period of freedom from respiratory symptoms. In an analysis of 107 cases of lung cancer at the Brompton Hospital, Davidson recorded a history of recent influenza in 20%, of pneumonia in 9%, and of bronchitis in 9%. In nearly all cases of this group cough is one of the first manifestations. Hunt avers that 36% of his 26 cases began with pain, probably due/

due to pleurisy over the growth, and contrasts this with the findings in tuberculosis in which pain is less common. In Davidson's series 16% originally came to notice as suspected cases of pulmonary tuberculosis. Sputum is usually absent at first but appears fairly soon after the development of cough, and slight haemoptysis or "streaking" is a variable additional feature. Pain in the chest may be one of the first symptoms but is more often associated with coughing. A certain number of cases present themselves with pleurisy. Davidson found 12% of cases where the onset seemed to have been the development of dry pleurisy, while 20% showed effusion. This is seen especially in pleural or peripheral growths and more rarely in mediastinal tumours.

Characteristic of the onset of malignant growths of the mediastinum is cough with gradually increasing dyspnoea, fleeting oedema of the eyelids and cyanosis. Recurrent attacks of fever have been noted over long periods in association with benign tumours. Bronchiectasis and chronic lung abscesses have frequently been present for years in the cases of benign growths.

(2) Cases with the slow onset of symptoms referable to other systems. This group is much smaller than the preceding one and forms one of the most notable/

notable though less common features of pulmonary carcinoma. The nervous system is the most frequently involved in this manner. Ferguson and Rees dealt with nine such cases at the National Hospital for Nervous Diseases during a period of three years. In their series the neurological manifestations occurred primarily in five, and simultaneously with respiratory symptoms in four instances. Three cases showed psychological changes, two suffered from Jacksonian epilepsy, and two from headaches and signs of increased intracranial pressure. Similar features were found in ten cases noted by Palmer and by Wetsler whom Ringer quoted at a recent discussion of the American Medical Association. Fried and Buckley recorded eleven of thirty-seven patients in whom a diagnosis of primary intracranial tumour was made, and on whom operation was performed. Of these, one showed symptoms for six years before the pulmonary lesion became manifest. It is noteworthy that brain abscess should receive little mention in view of the association of bronchiectasis with all types of tumour. Malnutrition and abdominal symptoms have occasionally been present for a considerable time before the causal lesion was discovered. This has also occurred in the benign cases. In one of Heuer's cases the appendix had been removed some years before extirpation of a mediastinal tumour gave permanent relief of symptoms. A patient who showed recurrent/

recurrent atelectasis was regarded as suffering from a neurosis until the condition was found by Myerson to be due to an intrabronchial fibrolipoma.

(3) Cases with sudden onset of respiratory symptoms.

A small proportion of all forms of intrathoracic tumour may begin with sudden and alarming symptoms. In some instances the sudden onset may have been preceded by minor disorders which had obtained no significance until a subsequent questionnaire was undertaken. "Thymic asthma" has already been mentioned as one form of sudden manifestation. Haemoptysis may occur rarely at the outset of symptoms of both benign and malignant tumours but it is more common to find bleeding at a later stage. Expectoration of the contents of a dermoid cyst has occasionally been the first indication of the lesion but again this is usually preceded by cough which may have escaped attention. Spontaneous pneumothorax has caused sudden grave symptoms. Heise and Trudeau noted this phenomenon in a man, aged 37 years, who had lifted a weight. At autopsy eleven months later an endothelioma of the pleura was found. Its occurrence in congenital cystic disease has already been described and it has been known to occur with other tumours. Massive collapse of the lung may be a rapid striking feature as in the case described by Ashbury in which it was the result of bronchial occlusion of a fibroma. The development/

development of fever may occur suddenly in association with suppurative or inflammatory complications but without the rapidity of the other features which have been mentioned.

(4) Cases in which the onset is sudden but without definite reference to the respiratory system.

Examples of this group are comparatively rare and their interest lies chiefly in their dramatic nature rather than in their practical value. Again most cases of this group are found to be of carcinoma of the lung with metastasis in the nervous system. Sudden hemiplegia and convulsions have been met with. The development of coma may be the only indication of disease. Symptoms suggesting acute encephalitis or transverse myelitis may become apparent fairly quickly. In six of eight cases of this nature recorded by Ferguson and Rees the onset was sudden, the speech being affected in five instances. In several of the cases of Fried and Buckley sudden paralysis of a limb or sensory disturbance was noted. Acute intestinal obstruction has arisen on at least two occasions as a result of intestinal metastases. Other irregular manifestations may be quoted but their extreme rarity does not warrant any compilation.

TABLE X.

CLINICAL FEATURES. CANCER OF THE LUNG.

Author	No. of cases	Cough	Dyspnoea	Sputum	Pain	Fever	Haemoptysis	Fatal	Loss of weight	Nervous Symptoms	Nervous symptoms only	Vocal Cord Paralysis	Pleural Effusion
Shennan	15	5	3	3	7	3	5	1	4	5	3		
Playfair & Wakeley	4	4		4									
McCrae, Funk,(2) & Jackson	14	14		12	11								
Hunt	26		3		9		12	2			2	7	12
Schuster	29						18						22
Parish	32	30	8		15	28	12				1	3	7
Vinson, Moersch & Kirklin	29		15		14	10	18				1	4	3
Barron	13	9	7		6		5		7				6
Eloesser	19	15	7	6	10		14	1					10
Grove & Kramer	24	20		14	13	8	5						
Maxwell & Nicholson	100	91	73		7	43	55 (1)	2		15		16	24
Simpson	139	92	70	70	89	54	50		72			24	39
Fried & Buckley (3)	37									11	11		
Miller & Jones	32	30	21			24	20		25				6
Total	513	310	207	109	181	170	222	6	108	31	18	54	129
Total of Cases with specific symptoms cited		392	405	215	412	371	469		199	152	139	326	419
% Incidence		79%	51%	50%	44%	46%	47%		55%	20%	13%	16%	30%

(1) Haemoptysis 55. Frank blood in 18 cases.
(2) Series diagnosed by bronchoscopy, mostly in early stages.
(3) Included in point of nervous manifestations.

TABLE XI.

MEDIASTINAL TUMOURS. CLINICAL FEATURES.

Author	Cases	Type	Cough	Dyspnoea	Pain	Haemoptysis	Hair etc. in sputum	Fever	Effusion	Empyema			
Hertzler	73	Dermoid	Most cases	23	28	Fatal 2	8						
Morris	57	"		9	5	5 5	20						
Lewald	3	"	1		1	1		1					
Heuer	5	"	3	1	3	1		1		1			
Smith & Stone	(1) 2	Teratoma	Recent pneumonia 2	1					2				
A.T. Edwards	4	"	3		3	2					Dysphagia	Oedema of face or limbs.	Enlarged cervical glands.
Shennan	2	Malignant.							1	1			1
Duguid & Kennedy	2	"	1	2							1	1	2
Helvestine	2	"	2	2							1	2	2
Ewing	3	"	1	2				1	1			2	3

(1) One case showed malignant changes.

COUGH. Nearly all patients suffering from intra-thoracic neoplasms complain of cough. In most it is the first symptom, in others it develops during the course of the disease and in a few cough does not occur. Usually dry and of an irritating nature in the early stages it may later be paroxysmal or persistent and accompanied by expectoration of sputum. Where there is pressure on the trachea, as occurs in thymic tumours and mediastinal growths, the cough is often of a brassy hollow character and resembles that associated with an aneurysm. Primary or secondary involvement of the pleura may cause a persistent cough accompanied by pain, which tends to diminish after the development of an effusion. When bronchiectasis is present the cough is characteristically worse in the mornings and is associated with purulent sputum.

SPUTUM. In the early stages of both benign and malignant growths the sputum is usually scanty. Later it may be copious. In cancer of the lung the sputum frequently contains blood in varying quantities, often at an early period and invariably in the later stages. The blood may be evidenced by constant staining or by repeated frank haemorrhages. Where bronchiectasis or lung abscess are present the sputum becomes purulent and/

and copious. This feature may be present during a period of months or of years and may be the sole indication of the presence of a neoplasm. In the more rapidly growing tumours such as the thymomata there is usually little or no sputum. Rarely the nature of the growths may be recognised by portions of tissue or other materials in the sputum. Schuster found carcinoma cells in three cases. Ewing mentions the expectoration of portions of a liposarcoma. Hairs and fatty matter indicate a communication between a dermoid cyst and a bronchus. This was noted in twenty of Morris' fifty-seven cases. The appearance of these substances may be sudden and alarming where rupture of a cyst or abscess has occurred.

DYSPNOEA. It is difficult to obtain a clear view of the incidence of this symptom. It is invariably present in some degree in most systemic diseases, and more especially is it associated with intrathoracic lesions. Though the standard has considerable variations it may be assumed that the mention of dyspnoea in the symptomatology of a particular case will indicate that some difficulty in breathing has been a prominent feature. The forms vary from breathlessness on exertion and stridor to extreme distress. Dyspnoea is found most commonly in mediastinal tumours producing/

producing obstruction of the air passages and more especially of the veins.

In cancer of the lung dyspnoea may be a fairly early feature and it may be out of proportion to the physical signs. It sometimes occurs in paroxysms and may be incited by rapid movement or by change of position. Some degree of breathlessness is noted in more than half the cases at a moderately early stage, and it becomes more marked during the process of the disease. In malignant tumours of the anterior mediastinum dyspnoea occurs early, usually in association with cyanosis of the face, and becomes a most distressing feature in almost all of these cases. Stridor is invariably found in these growths and is especially common with other thymic enlargements. Paroxysmal difficulty in breathing has produced death in a number of such cases. Dyspnoea is less common in some of the peripheral tumours and in the benign growths, though Hertzler recorded fatal dyspnoea in two of his series of 73 dermoid cysts.

PAIN. Though some cases of lung cancer have pain as an early symptom it does not usually occur until the disease is well established. Pain is often absent and its presence commonly indicates involvement of the pleura by the tumour. It may be associated with cough/

cough and with muscle spasm. The nature may be dull and localisation may be indefinite. Involvement of the pleura usually produces pain of a sharp lancinating character, while compression of the phrenic nerve may lead to pain in the shoulder region. Erosion of bone by malignant growth or from the hyperaemia associated with pressure by a benign tumour may result in pain of a constant boring type. Metastases in the vertebrae are often associated with agonising "girdle" pain, which Maxwell and Nicholson noted to be present in 5 of their 100 cases of lung cancer. The dermoid cysts and teratomata, and more rarely the thymic growths, do not usually cause discomfort. Occasionally pain may be referred to the abdomen. As a general rule however, it is not a common early feature of intrathoracic tumours and its presence is usually indicative of spread of malignant disease to the pleura, to nerve involvement, or to such secondary lesions as pleurisy.

HAEMOPTYSIS. The finding of blood in the sputum has hitherto been so intimately associated with pulmonary tuberculosis, of which it has often been taken as almost presumptive evidence, that other sources have been overlooked. Haemoptysis is occasionally the first symptom of cancer of the lung, and more than half the cases have definite haemorrhage at some stage. Bleeding/

Bleeding also occurs in cases of benign intrathoracic tumour. Five of Morris' series of 57 dermoid cysts died as a direct result of massive haemorrhage, the death resulted similarly in at least six cases of lung cancer out of the series of 222 patients demonstrating haemoptysis (Table X). In some instances repeated losses of moderate amounts of blood have lead to severe anaemia. Rare in benign tumours, and unusual in malignant growths of the mediastinum, haemoptysis is almost unexceptional and frequently occurs at an early stage of pulmonary carcinoma.

Loss of Weight and Weakness. Loss of weight is an infrequent symptom of intrathoracic tumours. Even in cases of lung cancer which are well advanced it is a noteworthy fact that most patients present less of the wasting and cachexia than is present with malignant disease elsewhere. Indeed it may be stated that many instances of benign intrathoracic tumour show more evidence of loss of weight and general toxaemia than is found in individuals suffering from cancer of the lung. Where, however, pulmonary carcinoma has been of slow growth, and especially where there has been resulting bronchiectasis, lung abscess, or empyema, the appearances of toxaemia are correspondingly/

correspondingly greater, and, in advanced cases, there may be considerable emaciation. Most of the malignant growths of the anterior mediastinum produce rapid loss of weight in association with great respiratory distress and slow asphyxia.

FEVER. When suppuration is present in a tumour or in the surrounding tissues fever may occur. Many cases of all types develop an attack of pneumonia as an initial feature. This may be followed by a period of apyrexia before other symptoms suggest the presence of an intrathoracic growth. Many of the benign tumours produce recurrent attacks of fever, and where suppurative complications are present fever may be constant. In 43 of 100 cases of lung cancer Maxwell and Nicholson found definite pyrexia. In Simpson's series of 139 examples of which 78 showed bronchostenosis and 16 had abscesses, fever was found in 54 instances. Night sweats are not uncommon in the suppurative complications and, like haemoptysis, are often attributed to tuberculosis.

NERVOUS SYMPTOMS. In cancer of the lung nervous phenomena may be due to cerebral metastases without any evidence of thoracic disease. Various observers have quoted examples of this syndrome. In a series of 139 cases (Table X) where this feature had been noted, symptoms/

symptoms due to central nervous involvement alone were recorded in 18 cases (13%). Nervous symptoms were noted in roughly 20% of cases of lung cancer. The forms which they have taken have already been mentioned and will be enumerated briefly. Psychological disorders were found in three of the cases of Ferguson and Rees. Jacksonian epilepsy has occurred in a few instances. Motor and sensory disturbances may be evident as pareses and tingling sensations in the limbs, and hemiplegia is occasionally produced. Affections of the speech have been recorded. Coma may occur with alarming rapidity and may resemble that following meningitis or encephalitis. Symptoms of cerebellar tumour may also be found. Evidence of lesions of the spinal cord is less common and is invariably due to metastasis in the bone or to benign growths producing compression from without rather than to secondary growths within the cord itself. Paresis of the legs, incontinence and other nervous disturbances have been recorded. The peripheral nerves are rarely affected. Hoarseness resulting from paralysis of the vocal cords is not unusual in malignant growths of the lung and mediastinum (16% in cancer of the lung) but is an occasional manifestation of benign tumours. The phrenic nerves may be involved with resulting pain in the shoulder and paralysis of the corresponding half of the diaphragm. The cervical sympathetic fibres are less commonly affected/

affected and Horner's syndrome is exceptionally found. In a case of intrathoracic fibroma recorded by Roberts there had been sympathetic paralysis of the face, eye, and arm for seventeen years. Involvement of the intercostal nerves is rare but may cause severe pain. Herpes Zoster has been seen as a result of this occurrence. The vagus nerves are rarely involved though dyspepsia may result from their affection, from cerebral metastases, or from toxaemia. The laryngeal disorders will be mentioned later.

The remaining symptoms will be dealt with briefly as they are less common and less constant for the various types of tumour.

CYANOSIS. In malignant tumours of the anterior mediastinum cyanosis is usually present in association with prominence of the superficial veins, and with dyspnoea, and may vary in degree according to position. In other types cyanosis is uncommon except as a terminal feature.

OEDEMA. In the thymomata oedema of the eyelids may be fleeting in the early stages, but later the face and one or both arms may be greatly swollen.

Oedema is occasionally seen in advanced carcinoma of the lung.

HOARSENESS. Involvement of the recurrent laryngeal nerves was noted in 24 out of the 139 cases of lung cancer/

cancer recorded by Simpson, and in 16 of Maxwell's series of 100 cases. From Table X, paralysis of the vocal cords would appear to occur in about 16% of cases of carcinoma of the lung. Hoarseness, not usually an early feature of lung cancer, occurs not infrequently with thymic tumours and very rarely with other types of growth. Adler states that lung tumours usually involve both nerves in contrast to aneurysm of the aorta which commonly affects the left nerve only. In Maxwell's series the right cord was paralysed in eleven and the left in five cases. Hoarseness may also be due to laryngitis resulting from coughing.

DYSPHAGIA. Complaint of difficulty in swallowing is rare except in malignant tumours of the thymus and of the mediastinum and in advanced cases of lung cancer. It has occurred in a few of the cases of benign tumour.

ENLARGED GLANDS. The supraclavicular glands are enlarged at a comparatively early stage in the case of the thymomata and lymphosarcomata. The axillary glands may become involved at the same time or at a later period. Glandular enlargement is much less common and is a later feature of some cases of carcinoma of the lung.

PHYSICAL./

PHYSICAL APPEARANCES.

It has already been shown that carcinoma of the lung may reach an advanced stage without any striking outward evidence of its appearance. Conversely, some benign tumours may lead to considerable physical deterioration. Loss of weight and emaciation are not usual until the late stages of lung cancer unless toxaemia has resulted from a suppurative condition. Rapid loss of weight occurs more commonly in the thymic growths. Anaemia is uncommon unless there has been considerable or repeated haemorrhage. Cyanosis does not occur unless mediastinal involvement has caused compression of the large veins or with extensive pulmonary consolidation. Cyanosis and oedema are present at a much earlier period, and to a greater degree, in cases of thymic and anterior mediastinal tumours and prominence of the superficial veins of the axilla and front and side of the chest, great anxiety of expression, and enlargement of the cervical glands may be striking features.

Clubbing of the fingers occurs in less than a quarter of all cases of intrathoracic tumours and is especially associated with added suppurative complications. Pseudo-hypertrophic pulmonary osteoarthropathy is rarely mentioned but has been seen in a/

a case where bronchiectasis and abscess were absent. Alterations of the shape and size of the pupil, and differences between the pulses may occur in any type of growth, but they are uncommon features. Obvious enlargement of regional glands has already been mentioned in association with malignant mediastinal tumours but is rarely seen in lung cancer. Chronic sinuses result from malignant infiltration more commonly by the thymic growths, but they may follow empyema. Some of the benign tumours may give rise to swellings in the subcutaneous tissues. Deformities such as scoliosis have been seen in association with dermoid cysts and teratomata, or have resulted from chronic empyema.

PHYSICAL SIGNS.

The physical signs show such wide variation according to the nature and site of the tumour and to the associated phenomena that any discussion on this aspect must necessarily be on general lines. Davidson has found that 12% of cases of lung cancer show signs of a dry pleurisy in the early stages, and that 20% of his series had evidence of pleural effusion. The latter is frequently present (30%, Table X), and according to several authorities thickened pleura is a common finding.

The/

The early cases reporting with cough and perhaps a little sputum may show slight diminution of movement of the affected side and there may be slight change of percussion note. In such cases auscultation may reveal some slight reduction of breath sounds, and rhonci and fine crepitations may be heard over a localised area. Where stenosis of a bronchus has produced atelectasis of a lobe or lobes there will be diminution of movement and of the size of the interspaces, dullness on percussion, diminution or absence of breath sounds and, what is a most important feature, deviation of the apex of the heart towards the affected side. Such features may be a prelude to the development of bronchiectasis.

A considerable proportion of cases of lung cancer are first seen at a stage when pleural effusion masks the underlying lesion. Effusion may occur on the side other than that of the tumour, or fluid may be evident in both cavities. In 184 cases of Maxwell's series, there was an ipsolateral effusion in 34, and a contralateral effusion in 7 cases. In lung cancer the fluid is haemorrhagic in about a quarter of the instances. Beal found one of four, Parish four of seven, Schuster 4 of 22, and Hunt 5 of 12 patients with effusion to have sanguineous fluid.

Basal/

Basal dullness may occur on the right side and a tympanitic percussion note may result on the left side from phrenic paralysis. In 16 of 100 cases recorded by Maxwell and Nicholson there was definite paralysis of the phrenic nerve. In later stages of lung cancer the physical features vary widely and are proportionately confusing. Pleural effusion is commonly evident and consolidation of some portion of the lung in relation to the growth is usually present. Increase of para-vertebral dullness may indicate involvement of the mediastinum. The characters of the pleural fluid will be discussed with regard to the diagnosis of intrathoracic tumours.

Growths of the anterior mediastinum are often evident by signs of pressure on the superior vena cava, by increased paravertebral dullness, and by enlargement of the supraclavicular glands. Local bulging in this region is occasionally seen. The benign tumours may be evidenced by areas of dullness which correspond to their site but the association of pleural effusion, bronchiectasis, and other complications will necessarily modify the physical features.

COURSE AND DURATION OF DISEASE.

The course and duration of each type of tumour depend on all the factors which have already been indicated and which may influence the manifestations of/

of the disease. Variability is extreme and only a generalisation is possible.

Carcinoma of the Lung and Pleura. Rough estimations concerning the duration of illness in these cases may be quoted:- Shennan - 5 months; Barron - 3 years to 6 months; Grove and Kramer - 1-8 months; Eloesser - 4 months; Hunt - 6½ months from onset until death. Kikuth found the average total duration to be 6 months - 1 year; growths occurring in young subjects having a shorter course. Davidson records the average period from admission to hospital until death as about 8 weeks. Brunn has recorded a table of duration of symptoms in 297 cases of his series of 626 pulmonary cancers - 6 months and less - 133 cases; 6-12 months - 90 cases; 12-24 months - 54 cases; 2-3 years - 8 cases; 3 years and longer - 12 cases. Of this total, in 80% symptoms lasted a year and less, and 50% had a duration of less than six months.

Thus it is evident that the majority of cases of lung cancer have a duration of about six months from onset until death. The course has been indicated in the section on symptomatology. Emaciation may be extreme in some cases but is not marked in the majority. Cough and expectoration of sputum increase in severity and amount and in nearly all cases there is some degree of haemorrhage. Pleural effusion usually develops

before death in those cases which did not present this feature at a previous stage, and in many the effusion becomes haemorrhagic or purulent. Pericarditis is often associated. Cyanosis and dyspnoea may become extreme and oedema of the limbs and ascites may occur. The termination may be rapid and early as a result of massive haemoptysis. Where symptoms are due to metastatic growths a corresponding course may follow and the pulmonary lesion may remain silent or may be disclosed shortly before death. Where the course has been of long duration it may suggest the presence of a slow growing neoplasm or malignant change in a benign growth.

The malignant mediastinal tumours are usually more rapidly growing and the duration of disease is short. Occurring most commonly in the second and third decades the duration varies from a few weeks to a year or longer. Slow asphyxia is characteristic, and cyanosis of the face and upper limbs with subsequent oedema gradually becomes more marked. Dyspnoea may be extreme and associated with great physical and mental distress. Pleural effusion often occurs. Enlargement of the regional glands is frequent and ulceration of the skin may be seen. Death usually follows a terminal attack of bronchopneumonia.

The benign tumours may be present within the thorax/

thorax for many years and even until death without the production of symptoms. Those which do show some manifestation invariably prove fatal, though the course may be long and determined largely by the complications which are produced. Morris showed that the duration of symptoms in his series of 57 dermoid cysts was:- 0-1 years, - 7 cases; 1-5 years, 10 cases; 5 years and more - 12 cases. The symptoms may gradually increase in severity or may show periodic remissions. Heuer's observations may be quoted as a summary! "The experience of the literature is overwhelming to the effect that, if untreated, the group of dermoid cysts sooner or later give rise to symptoms threatening life, and in the vast majority of cases causes death." With some reservation this statement may be applied to most of the benign intrathoracic neoplasms and cysts.

D I A G N O S I S.

The methods by which the diagnosis of intrathoracic lesions may be ascertained are numerous, and the combination of evidence from each of these means may be more complete than is obtained in the investigation of disease within the abdomen or within the cranium. The many measures which may be taken and the correlation of the various findings provide a study of greater interest and fascination than exists in the determination of diagnosis of disease in other situations. Careful investigation and thoughtful sifting of evidence are of vital importance in view of the dangers of acting on wrong assumption with regard to the nature and site of intrathoracic tumours.

In the first instance the various methods of investigation will be described, and secondarily the main features concerning the differential diagnosis will be discussed. With regard to the radiological aspects it is not intended to give more than the essential details.

What is generally referred to as the ordinary physical examination is a primary and essential point in the investigation. As regards the general features the state of nutrition, the colour, the hands, and the size of the pupils should be noted. Local inspection includes/

includes the consideration of the size, shape and symmetry of the chest, the condition of the superficial veins, the character of the breathing and the symmetry of movement. The latter is confirmed by palpation of the chest. The location of the apex of the heart is an important step. The sound conduction must be ascertained and the cervical and axillary lymph glands are palpated. The radial pulses should be compared with regard to regularity, synchronism, and equality of pressure. Percussion of the thorax will indicate to some extent the nature and site of changes which may have occurred within but more often attention is drawn to secondary effects of the tumours than to the growths themselves. Auscultation of the thorax is perhaps less helpful but the findings must be correlated with other signs. Thorough examination of the other systems is to be regarded as a routine procedure and, in view of the frequency with which metastatic growths develop in the central nervous system, special attention should be directed to it.

Microscopical examination of the sputum should be carried out. Schuster has recommended thionin blue as a stain which readily demonstrates carcinoma cells. The discovery of tubercle bacilli does not exclude the presence of other lesions. The Wassermann reaction of the blood may be of the utmost value though a positive finding does not necessarily indicate a syphilitic origin of a tumour. Examination of the blood may provide

useful information especially in connection with leucaemia and with echinococcal cysts. Where a pleural effusion is evident the fluid should be aspirated and examined. Blood is found in about a quarter of the cases of carcinoma of the lung with effusion, and more often in pleural tumours. Tumour cells may be seen and the finding of columnar or spindle cells may help to secure a diagnosis. Graham mentions the method of examination employed by Mandlebaum who fixes the sediment of the aspirated fluid by means of formalin. Opinions vary with regard to the value in diagnosis of the appearance of the various cells, mononuclear leucocytes, "signet ring" cells with fat globules, and other types.

Radiological examination may afford valuable information in intrathoracic disease where other clinical methods have been less helpful. The importance of this aspect of the investigation requires no emphasis, and without the aid of X-rays many pulmonary and extrapulmonary lesions would escape detection. Marked improvements in technique have enhanced the value of radiology, more especially in America, where there is perhaps a closer cooperation between the clinician and the radiologist. On these advances earlier diagnosis depends, and it is hoped that a more accurate correlation/

correlation may be established between the X-ray appearances, the clinical features, and the pathological processes, so that earlier treatment may be instituted.

The radiological findings are rarely pathognomonic of a specific lesion but the correlation of the results obtained by the various methods is often conclusive of the nature and site of an intrathoracic tumour. These methods will be mentioned and the significance of the findings will be discussed after which a broad outline of the more common appearances will be given.

Apart from simple photography and screen examination, stereoscopic films are of value and many workers have shown the necessity of films taken in the lateral and oblique planes. By forced expiration with the lungs filled and the exit of air prevented, the trachea and main bronchi are brought into prominence which renders easier the detection of abnormalities of outline or displacement of these structures. The instillation of lipiodol, now widely employed, has done much to make bronchography a recognised procedure in the diagnosis of intrathoracic lesions. By this means it is possible to show deformities or displacement of the bronchi and the relation of other shadows to the bronchial tree. Where the left lower lobe is concerned the administration of an effervescent drug such as a Seidlitz/

Seidlitz powder will increase the size of the gas bubble in the fundus of the stomach and, by the contrast which it yields, further evidence may be obtained of lesions in this situation. On the right side the induction of pneumoperitoneum has enabled differentiation to be made between lesions above and below the diaphragm. Similarly an X-ray photograph after artificial pneumothorax may indicate the presence or absence of pleural adhesions and may demonstrate the relation of the tumour to the lung. Where a pleural effusion is present information may be obtained from films taken before and after aspiration of fluid, and after replacement of the fluid by air. The barium meal may be of value in dissociating lesions of the oesophagus and of the fundus of the stomach.

A survey of the radiological findings in different types of tumour may now be made. It has been shown that in many instances of both benign and malignant growths, the secondary effects which may have been produced may mask the original features. Pleural effusion is one of the commonest findings in the more advanced cases of lung cancer, and produces a diffuse uniform opacity. Similarly the shadows cast by abscess, areas of atelectasis, or bronchiectasis, may be indistinguishable from those of the underlying tumour. In such cases bronchography may be helpful, and artificial pneumothorax may serve to render a tumour more obvious.

The opacity of the skiagram produced by atelectasis may be wedge-shaped with the apex at the site of obstruction. Where a whole lobe has become collapsed the shadow is more distinct, the mediastinum is displaced to that side and the corresponding half of the diaphragm is often elevated. An abscess may show a more or less diffuse shadow, and if there is communication with a bronchus a fluid level may be evident. With regard to the radiographic findings in carcinoma of the lung many writers have suggested classifications. Golden considered bronchial carcinoma in two stages; the first being associated with invasion, and the second stage that of stenosis with atelectasis and bronchiectasis. Melville has indicated three varieties: upper lobe carcinoma, with obstruction of the bronchus by a tumour, presenting a shadow due to collapse of the lobe, and defined by the interlobar fissure; hilar carcinoma with a shadow at the hilum radiating towards the periphery; and lower lobe carcinoma which produces irregular opacity and shows early invasion of the pleura. With some reservation and modification this classification holds with regard to the radiological appearance of most growths. In some cases however, the tumour may appear as a localised rounded shadow in the central region of a lobe and has been designated the parenchymatous type, as distinct from growths arising from the main bronchi.

A/

A diffuse shadow may represent massive involvement of a whole lung, and the opacity may be less dense in areas where necrosis has occurred. The rare condition known as lymphangitis carcinomatosa is evidenced by a diffuse mottling of the lung field by an opaque network. Involvement and paralysis of the phrenic nerve may be evidenced by the elevation and stationary condition of the lobe of the affected side. Instillation of lipoidol may show characteristic filling defect of the bronchus, and bronchiectatic cavities distal to the obstruction may be clearly depicted. This appearance is typical of broncho-stenosis caused by both benign and malignant growths. Artificial pneumothorax, in the absence of pleural adhesions and much surrounding consolidation, will show the collapse of healthy lung tissue in contrast to the unyielding part occupied by an intrapulmonary tumour.

Benign growths of the lung and mediastinum usually present a fairly opaque shadow of ovoid or spherical shape with a sharply defined margin. Those occurring in the lung are extremely rare and extrapulmonary tumours may be readily distinguished by the induction of pneumothorax which serves to separate the outline of the tumour from that of the collapsed lung. In the presence of adhesions which are frequently associated with the dermoid cysts collapse may not be successfully obtained/

obtained and the tumour is not so clearly defined. The opacity of the various types of growth is proportional to the density of their component tissues. Fibroma, chondroma, ganglioneuroma, neurofibroma, intrathoracic goitre, and solid teratoma all present dense shadows. Lipomata and dermoid cysts may produce only slight opacities. Secondary changes may mask the radiological appearances and bronchography may serve to distinguish and to localise a tumour.

Malignant growths of the mediastinum are usually characteristically represented by a diffuse irregular shadow appearing on both sides of the sternum, which may be confused with that due to an aneurysm of the aorta.

Bronchoscopy should be carried out in all cases where there is the suggestion of bronchial obstruction. The exact nature and site of the obstruction may be determined and the cause of symptoms may be deduced from the appearances which are evident. The diagnostic value of this method of investigation has not been sufficiently appreciated. Lilienthal states that bronchoscopy is probably the most important diagnostic aid that we have with regard to lung tumours.

In so many cases endoscopy is considered only as a last resort in diagnosis whereas the bronchoscope may be one of the most fruitful means in the investigation. In reliable hands there should be little danger/

danger. The discomfort resulting from bronchoscopy is comparatively slight and is out-weighed by the valuable information which it affords. McCrae, Funk, and Jackson, diagnosed bronchial carcinoma in 14 cases which they examined by this means. In nine instances examination of portions of tissue which were removed confirmed the diagnosis; two cases showed an appearance so characteristic as to render biopsy unnecessary, and in the remaining three cases the bronchoscope was not used because of the presence of metastases and abscess. The appearances which bronchial tumours present have been mentioned with the description of the morbid anatomy. The visualisation of a tumour, the nature which its appearance suggests, the fixation of the surrounding tissues and the lack of normal rhythmical movement, the character of the secondary changes, points of communication of an abscess with a bronchus, and deformities due to pressure of a growth from without the bronchial wall may all be determined. Biopsy is especially valuable in determining the histology of the growth and treatment may be immediately instituted when the nature of the condition has been decided. Finally it may be emphasised that bronchoscopy is an essential step in the early diagnosis of cases of bronchial carcinoma and may be useful/

useful in the treatment of both benign and malignant growths. Vinsen, Moersch, and Kirklin have indicated that secondary pulmonary tumours rarely produce bronchial stenosis and ulceration.

Thoracoscopy has not been widely employed in the diagnosis of intrathoracic disease and its use is somewhat limited, though as a means of treatment of pleural adhesions it has proved of value. Nevertheless, thoracoscopy does allow inspection of the surfaces of the lung and pleura and is a useful means of localising extrapulmonary growths, of indicating the nature of their attachments and the difficulties which may be met with at operation. The absence of adhesions betwen the pleural surfaces is necessary for the preliminary artificial pneumothorax. Tudor Edwards has illustrated the methods and results of thoracoscopy in an excellent article in the British Journal of Surgery.

Exploratory thoracotomy has hitherto found little favour as a final step in the diagnosis of conditions within the chest. The safety and ease with which exploration may now be carried out have removed some of the obstacles in the investigation which may not have been completed by the means already outlined. The examination of the thoracic cavity by an intercostal approach after the previous induction of pneumothorax has been shown to be free from difficulty and

to/

to be associated with less post-operative discomfort than an exploratory coeliotomy. Tudor Edwards has recorded two instances where malignant disease had been suspected and where thoracotomy revealed a teratoma which was successfully removed in each case. As a final step in the diagnosis of tumours, more especially of those situated at the periphery of the lung or occupying an extrapulmonary position, exploratory thoracotomy should be employed with greater frequency.

Mention may be made of the use of an exploring needle in the investigation of intrathoracic tumours. In a few instances information may be obtained and portions of tissue which are adherent to the needle may be examined microscopically. This method is not free from danger, however, and has little to recommend it.

Removal of enlarged lymph glands from the neck, axilla, or from other regions is rarely necessary as a means of diagnosis, but it may be of use where the nature of the disease is in doubt.

Differential/

DIFFERENTIAL DIAGNOSIS.

Some other conditions which may resemble intrathoracic tumours and which must be considered in their diagnosis will be enumerated and the main points of differentiation will be mentioned in each case. While it is impossible in some instances to draw definite points of distinction, the summation of evidence acquired during the course of examination will usually serve to distinguish the various lesions. For this reason benign and malignant tumours of the lung, pleura, and mediastinum are considered together in point of differential diagnosis.

Suppurative Conditions.

Chronic lung abscess is usually associated with the inhalation of a foreign body or may follow anaesthesia, operation, or pneumonia. Where there is communication with a bronchus the radiogram usually shows a fluid level in the abscess cavity and cinsiderable surrounding reaction. The appearance may be confused with a central carcinoma with necrosis, but the inner wall of malignant cavities shows a more irregular thickening and simple abscesses more often reach the periphery of the lung field. Bronchoscopy may demonstrate the presence of a foreign body in the type of abscess which follows its inhalation, and tissue removed may give definite proof of the presence of a tumour.

Bronchiectasis due to causes other than new growth tends to show remissions, and may be distinguished fairly readily both by the bronchographic appearances and by bronchoscopy, though it may be difficult to determine the cause if the condition is far advanced and if the secondary effects overshadow the primary lesion.

Empyema. Some cases of intrathoracic tumours are complicated by empyema and in these instances the primary lesion may be overlooked. In the diagnosis of tumour interlobar empyema may be especially confusing, but may be suggested by the clinical course and the radiological shadow situated in the interlobar sulcus. A chronic empyema may present an appearance similar to that of a dermoid cyst or teratoma both radiologically and at operation.

Mediastinal Abscess. The history of fever and pain, the leucocytosis and the relative acuteness of the condition may be distinctive but the later appearance may show great resemblance to that of a dermoid or teratomatous cyst.

Tuberculous Abscess. Arising from disease of the vertebrae, tuberculous abscess of the mediastinum is commonly associated with deformity, with spasm of the spinal muscles, and other typical signs. In tuberculous/

tuberculous pyothorax the previous history and clinical course will usually provide distinctive characters.

Non-Suppurative Lesions.

Chronic Bronchitis. The similarity of age incidence, the greater frequency with which males are affected, and the close correspondence between the symptoms may lead to difficulty in differentiation between chronic bronchitis and pulmonary carcinoma. Radiographic and bronchoscopic findings will remove any doubt in most instances.

Chronic Interstitial Pneumonia. It has already been shown that carcinoma is but rarely found in association with the various diseases, pneumoconiosis, asbestosis, siderosis, etc., grouped under this heading. This condition is bilateral and the X-ray appearances are usually sufficiently distinctive for diagnosis to be attained.

Pleural Effusion. Serous effusion may be confused with that associated with cancer of the lung and pleura. Examination of aspirated fluid may reveal tumour cells and in malignant disease the fluid is more often haemorrhagic. X-ray photography after aspiration, especially after replacement of the fluid by air, may reveal the shadow of a tumour.

Tuberculosis/

Tuberculosis. In many cases of phthisis, especially of the "closed" type without bacilli in the sputum, it may be impossible to differentiate tuberculosis from carcinoma. In the former the patients are usually younger and their appearance may suggest a tuberculous diathesis. Where a tumour is suspected bronchoscopy may be helpful especially with removal of tissue for examination. By this means many cases long regarded as tuberculous have had their true nature revealed. The central type of tumour may be confusing but here the radiographic shadow is usually denser. Cavity formation and serous or purulent effusion are seen in both tuberculosis and in cancer, and the occasional coexistence of both lesions must be borne in mind. The presence of tubercle bacilli in the sputum is diagnostic of pulmonary tuberculosis but does not entirely exclude the existence of a neoplasm. On the other hand, absence of bacilli from the sputum is presumptive but not conclusive evidence that the lesion is not of a tuberculous nature. The von Pirquet reaction is of little value in these cases but an injection of tuberculin may help to demonstrate the presence or absence of this disease. Scott Pinchin states that tuberculosis usually produces more wasting and other general symptoms in proportion to the signs.

Tuberculous adenitis may be confused with neoplastic/

neoplastic enlargement of the mediastinal glands but the former is more often found in young children. A cold abscess may occur in the mediastinum at any age. There is often X-ray evidence of affection of the lungs but this may be difficult to differentiate from spread of malignant disease. A tuberculous abscess has been mistaken for a dermoid cyst and the discovery of the real nature has only been made at operation.

Syphilis. Carcinoma and syphilis may coexist. Specific disease of the lungs may present all the signs and symptoms of new growth with evidence of tumour masses within the lungs, ulceration of the bronchi, and bronchiectasis. The finding of a positive Wassermann reaction of the blood should predicate anti-syphilitic treatment. Absence of improvement would afford some degree of proof of lung cancer. It has already been stated that the lung is not a common site of syphilis.

Actinomycosis. In the early stages it may be difficult to differentiate actinomycosis from carcinoma of the lung. Examination of the sputum may reveal the mycotic elements. Actinomycosis tends to present itself as a swelling of the chest wall and ulceration of the skin is not infrequent in contrast to lung cancer which rarely infiltrates the subcutaneous tissues. In the latter and in malignant mediastinal growths the regional glands/

glands are usually enlarged before surface ulceration has occurred. Actinomycosis of the mediastinum is usually the result of spread from the lungs or from the neck.

Hydatid Disease. Though this disease has in the main a regional distribution, the symptoms and signs may be confused with those of the rare simple cysts of the lung and mediastinum, and of dermoid cysts. In this country hydatid disease is uncommon. The characteristic globular shadow, due to the high saline content of the cyst, demonstrated by a radiogram is fairly distinctive and is less dense than the spherical form of carcinoma. Hydatid cysts, like dermoids, are prone to infection and diagnosis may only be made after such complication. Eosinophilia is not always found. The flocculation test may be of value and the intradermal reaction is said to be diagnostic by many authorities. Where rupture of a cyst has occurred and scolices have been discovered in the sputum the diagnosis will be simple. Hydatid disease of the pleura is almost always secondary to a cyst in the lung. Calcification of the cyst wall may cause some confusion from the radiological aspect.

Aneurysm. The distinction between an aneurysm of the aorta and a benign or a malignant mediastinal tumour is often difficult. The general arterial condition may be a helpful factor. Tracheal tugging is comparatively/

comparatively rarely caused by neoplasms. The extent of laryngeal paralysis may be a distinguishing feature. Aneurysm less rarely causes symptoms of irritation or paresis of the right recurrent laryngeal nerve. Expansile pulsation seen on the X-ray screen may indicate either tumour or aneurysm especially of the saccular type but films taken in lateral and oblique planes may serve to distinguish the two lesions. The signs of pressure on the venous trunks may resemble those found in the more rapidly growing lymphosarcoma group. A positive Wassermann reaction is suggestive of but a negative finding does not preclude aneurysm.

Carcinoma of the Oesophagus. Confusion may arise with regard to primary growths of the oesophagus and broncho oesophageal fistulae have resulted from tumours of both lung and oesophagus. In the latter dysphagia is usually an earlier and more prominent symptom. In most instances any doubt remaining after radiological investigation may be cleared by endoscopy.

Secondary Tumours. Metastases in the lungs are most commonly from the kidney, testicle, adrenals, the body of the uterus, the bones, and from melanotic growths. The primary neoplasm may be insignificant. In such cases diagnosis rests chiefly on the X-ray evidence. According to Melville, metastatic tumours are evident characteristically/

characteristically as rounded shadows, sometimes single but more often multiple, with the so-called "puff ball" appearance. Their multiplicity may cause confluence in which case the primary growth is usually manifest. Secondary growths are rare in the mediastinum except from the lung. Direct spread from carcinoma of the oesophagus causes confusion, but the history of dysphagia is rarely an early feature of primary mediastinal tumour.

Diseases of the Blood and Lymph Glands. With regard to lymphatic leukaemia the involvement of lymph glands is usually general and enlargement of the spleen is commonly present. The blood picture is generally distinctive but may be confusing in the aleukaemic type of this disease. The association of thymic enlargement has been mentioned. In myelogenous leukaemia the blood picture is characteristic. Hodgkin's disease may be difficult to differentiate from the more slowly growing types of mediastinal cancer but the Pel Ebstein temperature syndrome and the remissions suggest the former, and microscopical examination of an excised enlarged gland may be conclusive in both cases.

T R E A T M E N T.

Little more than half a century ago the surgery of the abdomen was at an early stage of its evolution, and operations such as resection of portions of intestine were regarded with wonder and were fraught with danger. At the present time the peritoneal cavity is explored and operations are performed on lines of simple technique with the assurance of safety. During the consideration of the means of diagnosis of some intrathoracic conditions it has been shown that exploratory thoracotomy is a procedure of utmost value and one which should be adopted much more frequently. The thorax has now become accessible to direct inspection and, in the hands of those who are familiar with the necessary technique, radical surgical treatment of lesions which have hitherto been regarded as entirely unapproachable may now be achieved. As recently as 1911, however, Adler remarked that operation was "so grave and hazardous that there can be but very few cases for which it would be suitable." Thus it is evident that more recent advances have altered to a great extent the opinions with regard to the means and merits of treatment.

It is beyond the scope of the present thesis to do more than indicate in a general way the results which have already been obtained by the various methods of treatment of intrathoracic/

intrathoracic tumours, the relative values of such means in specific cases, and the lines on which improvement and success may be achieved in the future. Only brief reference will be made to the technical aspects.

CANCER OF THE LUNG.

Heuer, Andrus, and Taylor collected from the literature thirty instances where malignant tumours of the lung had been subjected to operation. In most cases this consisted merely of partial removal of the growth or of drainage of an associated suppurative cavity. In seventeen examples complete removal of the growth was attempted, (Lenhartz 5, Kuttner 3, Heidenhain 1, Sauerbruch 5, Eloesser 1, Brunn 2), and in one of their own series Reid performed an incomplete extirpation, the patient remaining in comfort for two years subsequent to operation. Of these seventeen cases, eleven died from shock or pneumonia shortly after surgical intervention, one of Brunn's cases lived for five months, and one of Lenhartz' patients survived for one and a half years. Sauerbruch removed a tumour from the lower lobe of a patient who was alive and well five years subsequently, and in another case health was good three years after the removal of an extensive growth involving the lower lobe and the diaphragm. Kümmel excised the entire right lung in a patient, aged 56, but death occurred as a result of bronchitis in the/

the remaining lung. More recent publications include three cases of Tudor Edwards. In the first a carcinoma of a bronchus was dealt with by lobectomy, the patient being alive and well eight months later. An endothelioma of the right lower lobe was treated similarly, the patient remaining in good health twenty months subsequently. The same worker successfully removed the upper two-thirds of the left upper lobe including a secondary myeloma. This patient was known to be well three years later. Brunn performed a lobectomy in one stage but death occurred after one year had elapsed. Harrington has operated on fourteen cases of malignant pulmonary growth. Nine of these died from recurrence and one from cerebral embolism. In six cases partial removal only was performed owing to extensive infiltration. Four cases are still alive five years (sarcoma), one more than one year (squamous carcinoma), and two less than one year (adenocarcinoma) after operation. Cautery pneumectomy has not been given an extensive trial but Brunn employed this method in two cases.

With the aid of the bronchoscope intrabronchial carcinomata have been successfully removed by Greene, Keijser, Kahler, Chevalier Jackson, and Orton. In the last three instances the patient remained free from symptoms after $2\frac{1}{2}$, 11, and 4 years respectively.

Kernan/

Kernan and Cracovaner noted the presence of only scar tissue a year after repeated application of diathermy to a bronchial carcinoma and subsequent introduction of radon seeds through the bronchoscope. One of Ewart Martin's cases died of recurrence one year after removal of the growth followed by deep X-ray therapy.

Other forms of treatment which have been employed are radium and X-ray therapy. The former has been used with success, in association with the application of diathermy, by Kernan and Cracovaner. Tudor Edwards has described a means of application of radon seeds which are carried by a small hollow silver tube and inserted into the affected bronchus. The results of this method are as yet too recent for their value to be accurately estimated. Plaques of radium have been employed as a palliative measure in dealing with cases where malignant growth has become superficial. It has been found by Edwards and others that radiation by the bomb method has been of little use in preventing the spread of the growth, though Cade states that surface or distant application is the method most likely to be successful. In the cases of peripheral tumours, exposure and implantation of radon seeds has been favoured by success in the hands of Edwards, the tumour disappearing in three patients, one of which was in good health but developed hemiplegia about a year after

operation/

operation. In the experience of most workers deep X-radiation alone has shown few if any permanent cures. The success is variable and an estimate of the value of X-ray therapy may be obtained by quotation of the work which has been recorded. Hunt noted some temporary improvement in his series but the course of the disease was unchecked. Striking remissions were recorded in three cases and two patients experienced severe transitory reactions. Paterson has reported the results of treatment of 19 cases by high voltage X-rays. He found that life had not been prolonged, all the cases dying within 10 months, but that this form of treatment does give temporary improvement in advanced cases. Rist and Rolland employed radiotherapy in ten cases of which two showed some relief of symptoms, one neoplasm became broken up and toxaemia developed, and in the remainder there was no apparent effect. Two cases of bronchial carcinoma were reported by McCrae, Funk, and Jackson to be well two and three years after X-ray therapy. Lilienthal mentions the case of a man, aged 59 years, in whom the radiological appearance suggested extensive carcinoma of the upper right lobe with paralysis of the diaphragm. The symptoms, signs, and abnormal X-ray findings disappeared after exposure to deep X-rays, and the patient was in normal health nine months later(and remains well after five years - Heuer). The same author indicates the method/

method by which partial lobectomy may be combined with subsequent radiation through a large open wound, but he does not state any results of such treatment. Cooper has experienced somewhat encouraging results from X-ray treatment of 24 cases of primary carcinoma of the lung. Twelve patients showed no response, but all the others improved in general health and evidenced retrogression or arrest of spread. Six survived for 6 months, four for over a year, and two for more than two years.

As a result of a paper read by Tudor Edwards at the Annual Meeting of the British Medical Association in 1930, various workers have written on the subject of X-ray and radium therapy in malignant disease of the lung. Ffrangçon Roberts disputes the statement of Edwards that deep X-radiation has proved disappointing, and adds that he himself has dealt with cases which this form of treatment has benefitted by alleviation of symptoms and prolongation of life. Davidson states that no one of experience can be optimistic enough to suppose that the results are, at present, anything more than palliative, but that benefit has followed radiation and lives have been prolonged. Maxwell mentions his own results, which are comparable to those of Kidd in 1883, where the average duration of life was 14 months in sixteen cases treated by application of X-rays and 10.9 months in those untreated.

Chandler/

Chandler quotes the investigation of 120 cases of malignant intrathoracic tumour carried out by himself and C.T. Potter. Of 59 cases treated by X-ray therapy the only one which recovered was a mediastinal lympho-sarcoma with secondary growths in the neck. This worker bemoans the lack of success which has attended all forms of treatment, which should however be a spur to further effort in this direction. These views recently expressed are sufficient indication of the present position of X-radiation in the treatment of pulmonary cancer.

Coley's fluid has been used in a few cases and Lilienthal records two examples of sarcoma which were apparently cured by this measure. In one case lymph-angiosarcoma was diagnosed by removal of tissue during bronchoscopy and the patient showed no signs of re-currence after four years. Treatment by the exhibition of lead selenide or uranium salts may be mentioned but no marked success has followed this method and there are no records available to indicate its value.

The results already attained may now be summarised. Radical removal of tumours has been successful in a number of cases and would seem to be a propitious form of treatment especially if combined with implantation of radon seeds in carefully selected cases. Surface irradiation has not been effective in deeply situated growths/

growths. Deep X-ray therapy has been remarkably successful in a definite proportion and, like radiation from a radium bomb, has caused temporary improvement in a considerable number of instances, but it has not proved of definite curative value. Intrabronchial suspension of radium has not had an extensive trial but the results obtained are encouraging.

The lines of treatment which may be adopted in dealing with specific cases may be discussed briefly. In cases of localised tumours situated in the wall of a main bronchus fulguration by diathermy may be the most favourable method. Applications may be repeated until the growth is eradicated when radon seeds may be introduced into the tissues as a prophylactic measure against recurrence. Kernan and Cracovaner used three seeds and a total dosage of 9.3 millicuries. An alternative measure and one advisable in similar growths with greater extension is the suspension of radium in apposition to the tumour. Tudor Edwards inserts into the bronchus a small silver tube carrying eight radon seeds. The tube is suspended in situ for five to eight days before being withdrawn by traction on the thread which had been fixed to the cheek. Where the tumour appears to be localised to the central regions or to the periphery of the lung exploratory thoracotomy may be indicated. Secondary involvement of the mediastinal glands/

glands or wide local extension contra-indicates attempts at radical removal. Out of 118 cases seen by Tudor Edwards the latter procedure was regarded as justifiable in only three of nine cases submitted to exploration. In each instance removal was well justified by the apparent success which ensued. Radon seeds may be used in conjunction with radical operation and will help to diminish the chances of recurrence. Where spread of malignant disease has involved a wide area of the chest wall or where removal is not warranted on other grounds the insertion of radon seeds may be the method of choice. As a palliative measure in inoperable peripheral growths with firm adhesions radon seeds may be introduced by the same means as are used elsewhere. The association of artificial phrenic paralysis with radium implantation is advisable in order to diminish the activity of the lung and to lessen the tendency to haemorrhage. The rare operable tumours, defined by their apparent localisation and absence of metastasis, consist chiefly of peripheral or central growths, though early carcinomata of the larger bronchi have been successfully excised.
In view of the apparent failure of deep X-radiation and despite a considerable operative mortality complete lobectomy may be carried out in these cases. Where two lobes are involved both may be removed or the less affected/

affected may be partially excised. Radon seeds may be employed in association with radical measures either as a preliminary step or as a prophylactic measure against recurrence.

Unfortunately the cases which are at present classified as operable are extremely rare but the future of treatment would seem to lie in the use of radon seeds and in complete excision in selected cases. Where a lung tumour has appeared to be localised the operation of lobectomy has been successful in instances sufficiently numerous to warrant its continuation in certain cases. The prognosis of lung cancer is becoming more favourable especially in those instances where radium therapy and radical surgery may be combined.

Palliative measures are no less important as they must be adopted in the many cases where radical treatment cannot be undertaken Pleural effusion may be aspirated repeatedly to afford relief of dyspnoea. The drainage of empyemata and chronic lung abscess may help to reduce fever and discomfort. Such operations are in the main merely palliative but it should be remembered that these complications are often associated with benign tumours and, in spite of a provisional diagnosis of malignancy, subsequent improvement may be such that diagnosis and radical treatment of the underlying condition may eventually/

eventually be attained.

General therapeutic measures do not require more than brief mention. The use of morphia is generally necessary for the relief of distress. Pain due to pleural involvement may be relieved by the induction of artificial pneumothorax. Inhalation of oxygen is useful in combating cyanosis. Chandler has found the hypodermic injection of cocaene hydrochloride, gr.$\frac{1}{4}$, to be of marked benefit in cases of asphyxia due to advanced carcinoma.

BENIGN TUMOURS AND CYSTS OF THE LUNG AND MEDIASTINUM.

The rarity of benign tumours and cysts of the lung has already been indicated. It has also been strongly emphasised that these tumours may produce death after a long period of impaired health. Their benign nature in no way detracts from the severity of their effects, and for this reason their treatment is of paramount importance. With means and technique now at our disposal treatment has become increasingly successful.

With regard to the lung, there are on record at least fourteen cases presenting symptoms of varying severity in which cure has been achieved by the removal of/

of intrabronchial tumours with the aid of the bronchoscope. Death has undoubtedly resulted from a large number of similar benign growths when the diagnosis had been incomplete and where radical measures might have been successfully employed.

Borelius and Sjovall have enucleated a solid teratoma from the lung. In 1895 Pean exposed a cortical chondroma and employed a galvanocautery for its removal. The angioma discovered at operation by Tuffier was treated by application of ferric chloride.
A patient, from whose lung Lilienthal extirpated a cyst, tended to suffer from attacks of mediastinal flutter which were prevented by a permanent Thiersch "finger cot valve" placed at the opening of the fistula.

The treatment of benign tumours and cysts of the mediastinum is an important and successful branch of thoracic surgery. The hour glass tumours have already been mentioned. Instances of surgical removal of other types of simple growth will be enumerated. Jacobaeus and Einar Key removed two fibroleiomyomata from the posterior mediastinum. Heuer employed an intercostal approach for the extirpation of a xanthoma from the lateral thoracic region. By a two-stage operation with division of the manubrium sterni Dunhill removed a fibroma from the anterior mediastinum. Garré has removed two fibromata; the first, which was in two portions occupying the anterior and/

and posterior mediastina, through an intercostal incision, and the second, which was situated in the posterior mediastinum, by the posterior approach. Roberts recorded the removal of two, and Schwyzer of one fibroma. At least six lipomata have been extirpated, in most instances from the anterior mediastinum. Harrington records the operations for five neurofibromata, two fibromata, four teratomata, one osteochondroma and two other simple tumours. From his experience of operations on 28 examples of intrathoracic growth this observer points out that from the clinical history and from evidence obtained at operation there were indications that four malignant tumours had originally been benign (two squamous carcinomata from dermoid cysts, and two fibrosarcomata from fibromata) and emphasises the need for early operation in benign growths. Ganglioneuromata have already been mentioned and complete extirpation has been satisfactorily achieved by several workers, of whom Sauerbruch and Lilienthal amongst others employed the posterior extra-pleural approach. Thymectomy has been performed on many occasions but there are few instances of removal of benign tumours of the thymus. Intrathoracic goitre has usually been dealt with by extraction from above, a collar incision being adopted as in the operation for cervical goitre. Of the simple varieties of cyst occurring in the mediastinum Sauerbruch has removed two examples from the anterior mediastinum, and Clifford and Mixter extirpated in two/

two stages a large cyst from the posterior mediastinum. Tudor Edwards has removed a cyst which may have been a diverticulum from the pericardium.

DERMOID CYSTS AND TERATOMATA.

Heuer, Andrus, and Taylor investigated the literature prior to 1927, and a careful survey was reported as follows:- 135 cases of dermoid cyst of the mediastinum have been recorded. Of these, 46 died untreated and 69 were submitted to operation. Of the latter one was treated by simple drainage of the pleural cavity, 34 by incision and drainage of the cyst sometimes with marsupialisation, 12 by incomplete resection of the tumour, and 22 by complete extirpation. Of the 34 treated by excision and drainage only 5 were cured, and many others recovered but died subsequently or had permanent fistulae. Incomplete resection was performed usually in cases complicated by infection or where adhesions rendered complete removal unsafe, and nearly all the cases died subsequently, though several lived for years with fistulae and sinuses. Of the 22 cases where extirpation was complete, 20 cases were completely cured, one died from pericarditis, and one from sepsis. It is apparent from these observations that, apart from the ordinary operative mortality, complete/

complete removal wherever possible produced the most satisfactory results. This is borne out by the experience of other writers. Harrington, Tudor Edwards, and others have also recorded several cases. In many operation was performed in two or multiple stages which is an important feature of the technique. It is generally agreed that total extirpation of dermoid cysts and teratomata is the method of choice. In many cases however such a procedure is impossible owing to calcification or to close attachment of the growth to vital structures. Where infection is present drainage of the empyema or of the cyst may be necessary as a preliminary step and the tumour may be removed in stages. An adherent remnant of the cyst wall may be coagulated by the application of diathermy but caution is necessary in order to prevent necrosis of important structures and severe secondary haemorrhage. An alternative mode of treatment is the application of a chemical destructive agent. Where removal is delayed by sepsis and multiple stages, or where the cavity remaining after extirpation does not disappear, several plastic operations may be necessary. The modes of access and removal will be discussed later in the section on the technical aspects of treatment. X-ray therapy has been employed and some cysts have shown diminution in size after radiation but there has been no permanent curative effect.

ENLARGEMENT OF THE THYMUS.

Simple enlargement of the thymus may be present in children and in adults without the production of symptoms. O'Brien quotes Mosher, Macmillan, and Motley who found that 7.5% of 2,344 children showed a positive thymus shadow in radiographs and, after X-radiation of the mediastinum, all these cases underwent operation without a single instance of sudden death. O'Brien had similar experiences with 2,526 cases, and he states that, while evidence is lacking of enlarged thymus as an integral causative factor in sudden death, radiation therapy should be employed in children presenting X-ray evidence of the "broadened mediastinal shadow" without symptoms, for whom general anaesthesia is contemplated. In actual practice without other evidence routine radiography of the thorax is not carried out and such symptomless thymic enlargement is not discovered. Where it has been found however and anaesthesia or operation of some nature is necessary the child should be submitted to X-ray or radium therapy prior to operation. Kinney and Taylor have found that congenital heart lesions were responsible for the symptoms in those cases which did not improve after X-ray therapy and they draw attention to this means of differentiation.

In cases of simple thymic enlargement with symptoms of dyspnoea operative treatment has largely given place

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to radiotherapy. In 1896 Rehn treated a patient with severe dyspnoea by intubation through a tracheotomy opening. Removal of the tube produced recurrence of symptoms, and eventually, through an incision above the suprasternal notch, an enlarged thymus was exposed, drawn out of the mediastinum and sutured to the front of the manubrium with complete relief of symptoms. In a similar case König performed a partial resection and sutured the remainder of the gland to the sternum. In 1913 Parker collected records of 50 cases which had been submitted to operation, and found a mortality of 33% though in some instances death was due to other causes. In 1914 von Haberer reported satisfactory results in eleven cases where the thymus had been removed in association with goitre or where pressure or toxic symptoms had not been relieved by thyroid-ectomy. Halsted and Kocher had similar experiences. In cases of myasthenia gravis von Haberer, Schumaker, and Roth achieved success after thymectomy. Of recent years the surgical treatment of thymic lesions has had little prominence though Marique, in 1923, reported fifteen thymic resections for the relief of dyspnoea in children.

Friedlander, who has done much work on this subject, successfully treated by X-ray therapy a child aged two months who had suffered from constant dyspnoea and attacks of suffocation. Since 1904 Friedlander

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and Lange have dealt with 250 cases by this means, and record only two deaths in their series. Diminution of symptoms was noted in twenty-four to forty-eight hours after the first exposure. Herrick reports the results in six cases of young children. In three who were submitted to radiation recovery was satisfactory while death occurred in two cases untreated by this means. Radium may be employed as an alternative to X-rays. Singleton states a preference for the latter, while Heublein reports a series of cases successfully treated by radium the application of which is less terrifying to children.

From the results quoted the lines of treatment to be adopted would appear to be fairly well defined. In cases of extreme urgency with suffocation not responding to simple measures, intubation through the larynx or through a tracheotomy opening may be carried out. Where immediate steps are not indicated and the diagnosis has been confirmed by radiography radiation should be instituted. Heublein employs 200 milligrammes of radium filtered through .33 mm. of silver at a distance of $\frac{1}{2}$" from the skin. The tube is maintained for one hour in four different positions over the anterior aspect of the thymus producing a total dose of 800 milligramme hours. Friedlander and Lange apply filtered X-rays at a distance of 9" from the surface, in doses of 25 milliampère minutes for children

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over three months, and 15 milliampère minutes for younger subjects. Treatment is instituted at weekly intervals or may be carried out daily in urgent cases. Surgical removal is rarely required but may be necessary where there has been no response to radiation. Marique emphasised the simplicity of the operation through a low incision as for tracheotomy, as much of the gland as possible being shelled out. Veau, quoted by Lilienthal, advocates rapid exploration of the thymus in urgent cases, tracheotomy being performed where there is no apparent enlargement of the gland. In the rare cases of benign tumours of the thymus radical removal is the method of choice. The diagnosis, however, is usually a matter of the utmost difficulty and may not be completed until operation.

MALIGNANT TUMOURS OF THE MEDIASTINUM.

From a study of the literature it is difficult to obtain statistics concerning malignant tumours of the mediastinum especially with regard to the results of their treatment. It has been shown during the consideration of the pathology and clinical features that growth of these tumours is especially rapid in the small celled types which are the most common. As a result of this feature most of the cases present themselves after the condition has become well established,/

established, when growth has advanced to a considerable extent with involvement of distant glands in the cervical and axillary regions, and when the problem of treatment is consequently more difficult.

Radical surgery can play little part in the treatment of primary malignant disease of the mediastinum. The growth is usually so extensive that complete removal is generally speaking impossible. So far as can be ascertained only two cases of lymphosarcoma have been treated by surgical means with apparent success. The patient of Haines, who removed a mass of glands from the mediastinum, remained well until death from "brain trouble" two years later. Schwyzer quotes Marwedal who removed a malignant tumour of the anterior mediastinum the patient showing no recurrence over two years later.

X-rays and radium therapy have formed the most successful means of attack on this disease. Burnham noted continuous improvement for periods of months up to four years in seven of eight cases submitted to radium therapy and found that occasionally there was response to radium where X-radiation had produced no effect. Ewing has reported the apparent cure of one thymic tumour treated by heavy doses of X-rays. Janeway records nine cases of mediastinal growth treated by radium and X-ray therapy, in three of which the health/

health remained good, and in one only slight diminution in size of the mass occurred though the general health improved. This author claims that radiation produces the best results in lymphosarcoma. Evans and Leucutia have extended the exposures to all areas of the lymphatic system as well as to the mediastinal tumour. They gave a dose of 70% S.U.D. which caused disappearance of the largest of the tumours within ten days. and state that apparent cures have been obtained. In comparing the reaction of different types of growth these workers found the small round cell tumours to be the most favourable and most responsive type, the large round cell variety to show greater tendency to recurrence, and Hodgkin's tumours to require a period twice as long before disappearance occurs. In order to avoid the pleuro-pulmonary effects described by other radiologists the lungs were carefully screened. In dealing with lymphosarcoma Desjardins found that the enlarged lymph nodes melted away as a result of radiation in a manner not found in any other disease. Of four cases treated two were well five and three years later, one was well and still progressing favourably four years after the initial treatment, and the fourth, an advanced case, died in spite of disappearance of the signs of tumour. The latter occurrence has been noted not infrequently and has been attributed to anaemia

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and other general effects of radiation. Severe general reaction lasting for several days has been noted by Evans, Leucutia, and others, and is said to result from the liberation of toxins from tumour destruction. Carver has described the treatment of a malignant tumour of the thymus which occurred in a female, aged 39 years. During the course of two years forty applications of radium and X-rays were applied and growth was controlled. At autopsy all evidence of tumour had disappeared from the primary site and a large cavity in the right lung had probably been occupied by the neoplasm. Finzi agrees with most authorities in stating his belief that X-ray therapy is most effective in tumours of the lymphosarcoma type, and maintains that radium is the method of choice in those types which tend to be localised.

It is difficult to assess the relative merits of the different forms of treatment of malignant tumours of the mediastinum. There is not as yet an extensive publication of large series of results by which the value of radiation therapy may be estimated. From the opinions expressed by competent authorities deep X-ray therapy would appear to be the best line of treatment which may be adopted in growths of the lymphosarcoma type, which are usually more rapid in growth and which occur at an earlier age. Radium may be employed with advantage/

advantage in those cases which have failed to improve under X-radiation, and in the more slowly growing neoplasms which are mostly of the large cell type and which have a close resemblance in character to carcinoma.

With regard to the group of tumours probably originating from the chest wall, Tudor Edwards has removed "a plexiform sarcoma", but death was brought on by reactionary haemorrhage ten hours after operation. The same worker removed a large chondrosarcoma growing from the second and third ribs. Sauerbruch, Schede, and others have performed wide resections of the thoracic wall. Many of these cases have been followed by recurrence, and radiation has not yielded entirely satisfactory results. It would appear that excision with subsequent exposure to X-rays affords the best hope of success.

It is not intended to describe the technique of radiotherapy which is outside the scope of this work, but brief reference will be made to the practical and technical aspects of the surgical treatment of intrathoracic tumours.

Pre-operative Measures. Prior to operation the general condition of the patient is raised as much as possible. Rest in suitable environment reduces the tendency to post-operative bronchitis and other complications. Careful postural drainage of suppurative cavities,/

cavities, bronchiectasis, lung abscess, and empyema reduces the associated toxaemia. Blood transfusion may be helpful in the preparation of some cases. Many workers induce pneumothorax several days before operation. This procedure is recommended by Harrington and was carried out in each of the eighteen cases which he has described. Where thoracoscopy has been performed pneumothorax will have been instituted previously.

Anaesthesia. Various writers have indicated a preference for particular methods of achieving anaesthesia in thoracic operations. Where there is no prospect of the pleural cavity being opened simple open inhalation anaesthesia may be used alone or supplementary to local, regional, or spinal anaesthesia. Many cases may be dealt with to a considerable extent under local infiltration and nerve blocking. Spinal anaesthesia has not been adopted extensively. Of vapour anaesthesia, ether or nitrous oxide and oxygen are the most widely employed. Where there is some risk of tearing of the pleura or where access is by the transpleural route some form of positive pressure is essential. One of the most convenient means of applying positive pressure is a closely fitting mask into which a forced stream of vapour is passed. Intrapharyngeal anaesthesia/

anaesthesia is also useful in this respect. In those cases where both pleural cavities may be opened positive pressure anaesthesia by the intratracheal method is the one of choice. Where ballooning of the lung tends to interfere with access intratracheal administration is less effective and control of mediastinal flutter may be readily achieved by the close application of the mask as described above. Harrington has found ethylene anaesthesia to be effective.

Methods of Access. (1) For cervico-retrosternal tumours a low collar incision may be used. Where access is incomplete this may be combined with median section of the manubrium sterni and separation of one of the halves at the level of the second intercostal space as described by Sauerbruch. Bardenhauer has advocated the division of the sternum at the junction of the body and manubrium, the sternoclavicular joints, and the first two costal cartilages on each side. This method is more difficult to carry out and has not been widely employed. (2) Retrosternal tumours - Median sternotomy is the method of choice and involves vertical division of a portion of the sternum and separation by horizontal section at the required level. Milton originally divided the sternum throughout its length and this procedure may rarely be necessary. Modifications of this method have been adopted by

Aurousseau and others. Fontain, Ferrier, and Raymond used a curved incision reaching from the second to the sixth interspaces and a "trap door" approach which may be combined with lateral division of the sternum. Friedrich divided the sternum transversely and the costal cartilages above and below so that the two flaps of the sternum could be retracted. (3) Heuer, Duval, and Lilienthal obtained excellent access by means of a long intercostal incision and separation of the ribs by a rib spreader. This method may be combined with subperiosteal resection of one rib or with division of the posterior ends of several ribs. In older subjects in whom retraction of the ribs is more difficult resection of portions of several ribs may be carried out. (4) Access may be obtained to the posterior mediastinum by the extra pleural route through a curved incision one limb of which is vertical and parallel to the vertebral spines and the other curves laterally. One rib may be resected and Lilienthal advises the division of the posterior ends of the adjacent ribs which may be retracted and shingled over one another. Nasiloff, Bryant, Enderlen and others have advocated resection of the posterior portions of a number of ribs. By careful separation of the pleura access to the mediastinal structures may be readily achieved. This method has been frequently used and

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may be recommended. For purposes of localisation of structures a diaphane suspended in the oesophagus may be helpful.

A long intercostal approach has been employed by most workers in the operation for lobectomy. The alternative method of resection of several ribs may be necessary where the ribs are not easily retracted. Harrington, Brunn, and others advocate transpleural removal of tumours and lobectomy as one-stage operations. Where circumstances permit, this may be carried out and is especially feasible in children and where time is not prolonged and the shock is slight.
In cases where lobectomy is contemplated in the presence of infection the lobe may be freed and brought to the exterior at a first stage. The pedicle may be divided subsequently. Where infection is likely to be spread to the pleural cavity and adhesions have not already been formed operation should be in two stages. At the first the division of ribs is carried out and adhesion of the parietal and visceral layers of pleura is produced by tamponnage. At a later stage the pleura may be incised and a tumour exposed with less risk of spreading infection to the remainder of the pleural cavity. Morrison has advocated the cocainisation of the vagus plexus prior to lobectomy in order to avoid reflex cardiac inhibition. Morriston Davies has/

has adopted this precaution in several cases.

Drainage may be necessary after extensive removal of tissue and may be established by gauze packing or by a rubber tube passed through the wound or through a separate opening. Subsequent to operation effusion is a common occurrence and should be dealt with by repeated aspiration. Continuous suction has been found to be a great advantage in the relief of discomfort and difficulty in breathing. By this means any tendency towards valvular pneumothorax may be diminished.

No attempt has been made to do more than indicate the general lines on which the treatment of intrathoracic tumours may be carried out. Further details are beyond the scope of this work. The essential features are dependent on the judgment of the time which may be allowed and the degree of shock which may be safely produced. Of special concern are the rapidity of access and the number of stages. Many fatalities have resulted from prolonged exposure of the thoracic contents in a single operation where multiple stages would have lead to success.

SUMMARY AND CONCLUSIONS.

1. A survey has been made of the literature concerning primary intrathoracic tumours, and the series of recorded cases have been analysed in order to obtain detailed information of every aspect of both benign and malignant growths. With regard to the rare forms of neoplasm most of the examples which have been reported have been mentioned in this work.

2. While benign tumours are rare malignant growths occur with very much greater frequency than is generally realised and the incidence has shown a marked increase during the last few decades. It appears probable that this increase is to some extent real. Carcinoma of the lung is found in more than 8% of cases of cancer which are seen at autopsy and in more than 1% of all patients submitted to post-mortem examination. The lung is therefore a common site of malignant disease. Primary malignant disease of the mediastinum is correspondingly rare.

3. The average age at which pulmonary cancer occurs is 51 years, and the sex incidence is represented by 78% males and 22% females. Benign tumours may be/

be seen at any age, and the dermoid cysts and teratomata are usually manifest during the second and third decades of life.

4. There is no evidence of definite predisposing factors in the etiology of intrathoracic cancer though the recent increase has been associated with modern air pollution. Examples have been quoted of malignant transformation of benign growths.

5. Most varieties of simple tumour are found in the lung and in the mediastinum though they do not occur frequently. Carcinoma affects either lung with almost equal frequency, and there is no marked predilection for individual lobes. The gross pathological features have been described. The histogenesis of lung cancer has been discussed and the main histological types are ******* as follows:- squamous carcinoma 20%, polygonal and columnar cell growths 27%, and undifferentiated forms, including small round cell and oat cell tumours, 54%. Nearly all growths present cells of varying degrees of differentiation in association with the predominating type by which the tumour is designated.

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6. Of cases of lung cancer which present distant secondary tumours the metastases show the following distribution:- Extrathoracic lymph nodes 27%, liver 30%, bones 19%, suprarenal glands 15%, kidney 14%, brain 10%, and pancreas 8%. The methods of spread and the local behaviour have been described. Bronchiectasis is a frequent secondary effect of both benign and malignant neoplasms. Pleural effusion, which may be an early feature of pulmonary carcinoma, is seen in about a third of the cases of this disease and in most examples of primary growths of the pleura.

7. The pathology of enlargement of the thymus has been detailed and the histological features of the thymomata and lymphosarcomata have been described. It is concluded that many of the growths hitherto regarded as mediastinal sarcoma have arisen in the bronchi and lungs and are of the nature of carcinoma.

8. The clinical features of the various tumours have been detailed in correlation with their pathology. If untreated, the benign growths may produce severe symptoms and may cause death. In a definite proportion of cases of carcinoma of the lung there is little or no evidence of respiratory disturbance/

disturbance and symptoms may be due entirely to secondary growths, more especially to those affecting the nervous system. The duration of lung cancer is about six months from the onset until death though many cases show a longer course. Emaciation is not usual and is much less common than is associated with malignant disease in other sites.

9. The diagnosis of intrathoracic tumours may be difficult to achieve without thorough investigation. Bronchography and bronchoscopy should be employed more frequently, and exploratory thoracotomy should be undertaken in certain cases. By these means it may be possible to establish accurate diagnosis and to detect early lesions which would not be discovered by clinical examination or by simple radiography. The necessity for complete investigation is strongly emphasised.

10. Benign growths which have produced symptoms should be radically removed. The value of X-radiation in the treatment of lung cancer has not been fully established. Radical removal combined with radium application or radium implantation alone in selected cases would appear to/

to be the most propitious forms of treatment of carcinoma of the lung. The various methods have been outlined and some technical aspects of treatment have been mentioned.

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